

# Simple and expedient access to novel fluorinated thiazolo- and oxazolo[3,2-*a*]pyrimidin-7-one derivatives and their functionalization *via* palladium-catalyzed reactions.

Wafa Blancou,<sup>1,2</sup> Badr Jismy,<sup>1,\*</sup> Soufiane Touil,<sup>2</sup> Hassan Allouchi<sup>3</sup> and Mohamed Abarbri<sup>1,\*</sup>

<sup>1</sup> Laboratoire de Physico-Chimie des Matériaux et des Electrolytes pour l'Energie (PCM2E), EA 6299, Avenue Monge, Faculté des Sciences, Université de Tours, Parc de Grandmont, 37200 Tours, France.

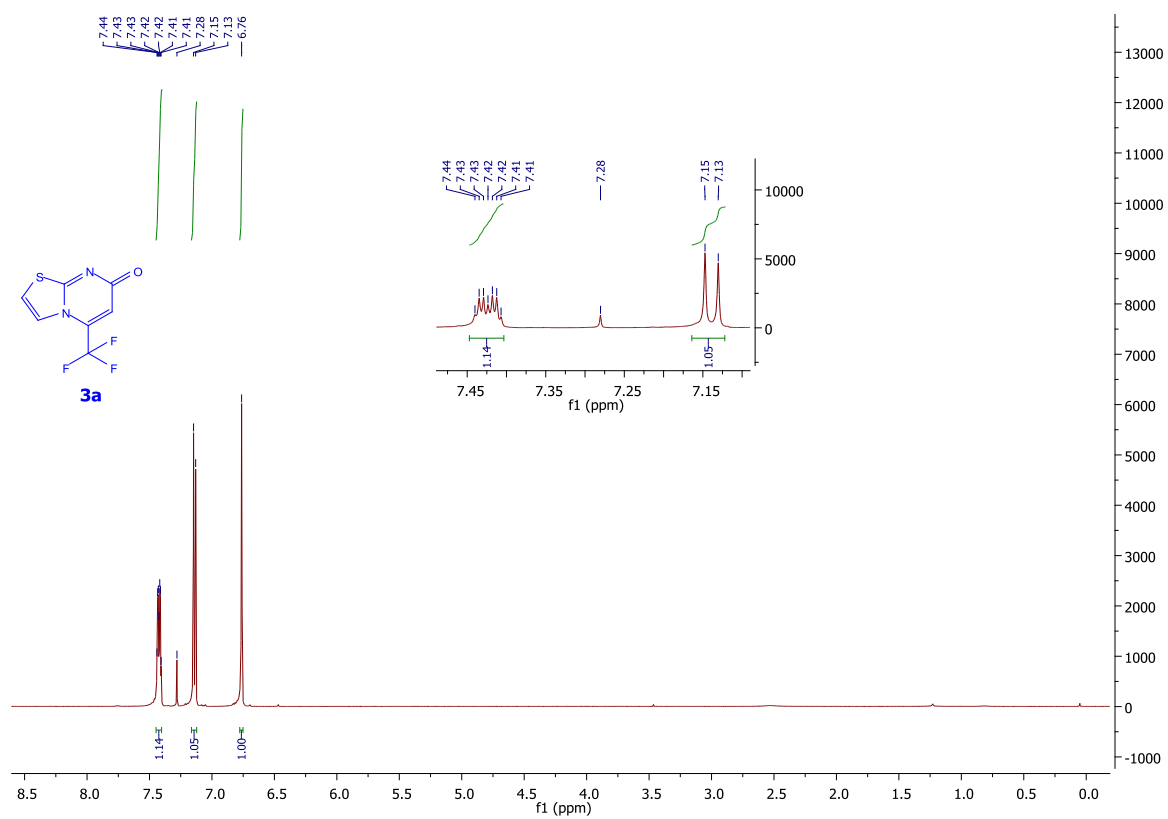
<sup>2</sup> Laboratoire des Composés Hétéro-Organiques et Matériaux Nanostructurés (LR18ES11), Université de Carthage, Faculté des Sciences de Bizerte, 7021 Zarzouna, Tunisie.

<sup>3</sup> Université de Tours, Faculté de Pharmacie, EA 7502 SIMBA, 31 avenue Monge - 37200 Tours, France.

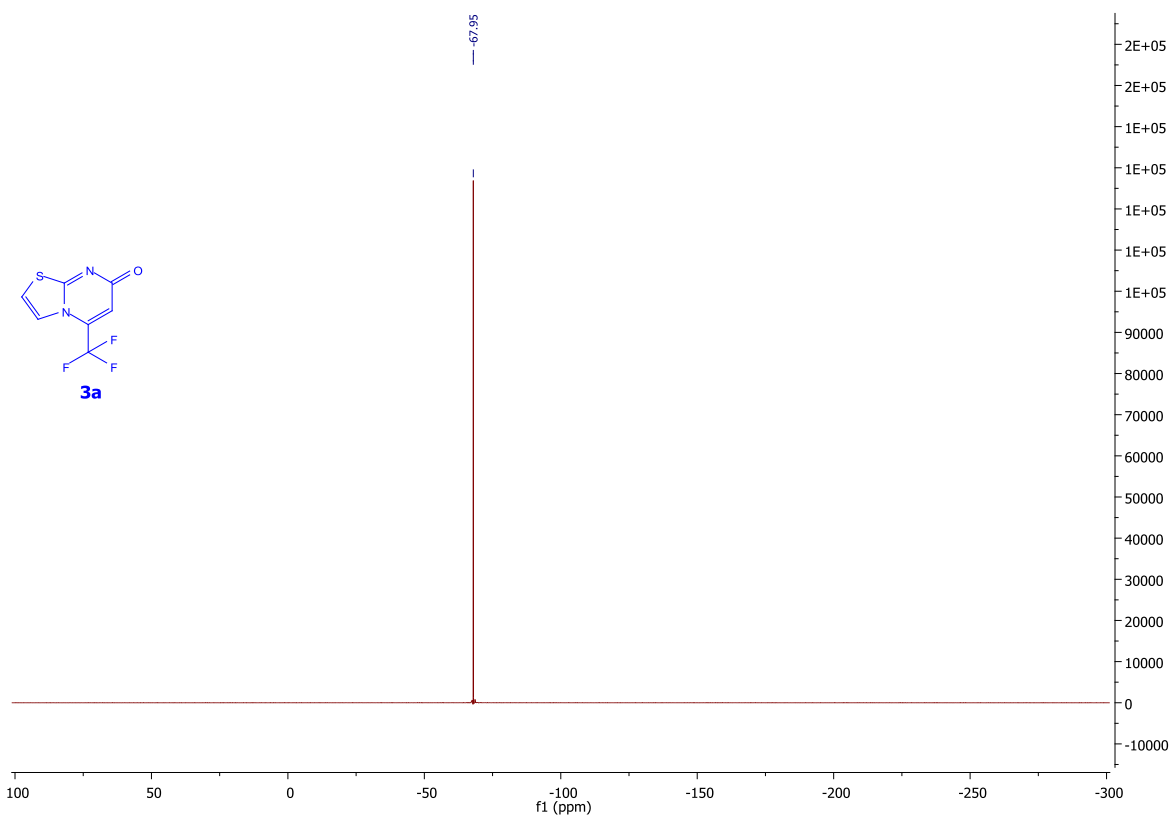
\* Correspondence: [mohamed.abarbri@univ-tours.fr](mailto:mohamed.abarbri@univ-tours.fr) and [badr.jismy@hotmail.com](mailto:badr.jismy@hotmail.com) ; Tel.: +33(2)47-36-73-59; Fax: +33(2)47-36-70-73

5-(trifluoromethyl)-7H-thiazolo[3,2-*a*]pyrimidin-7-one (**3a**).

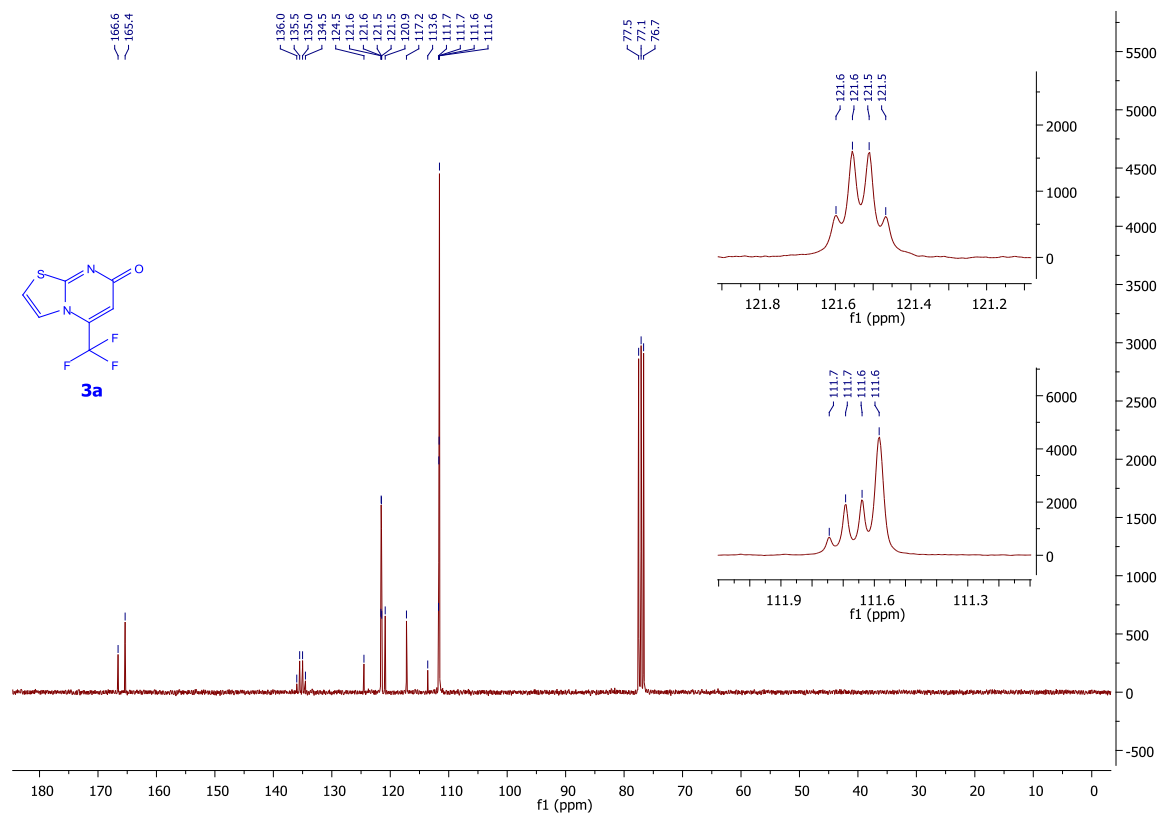
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)



**<sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>)**

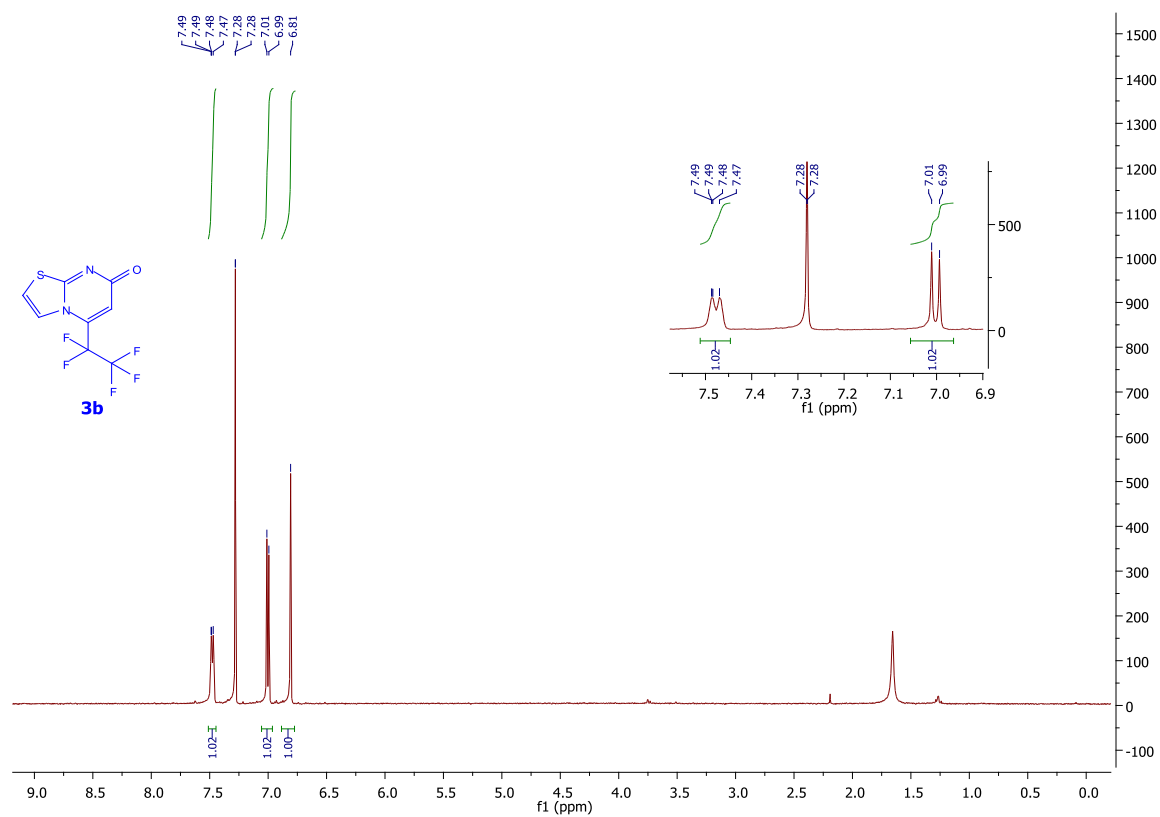


**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)**

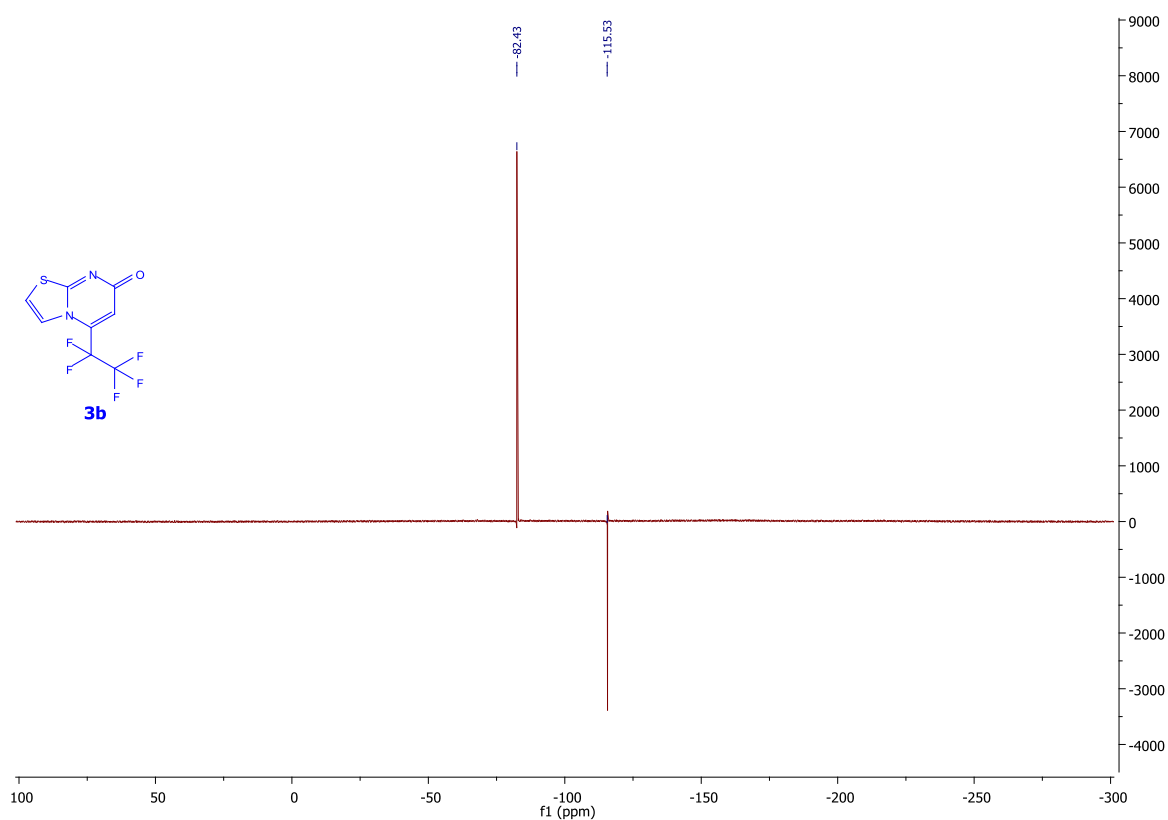


5-(perfluoroethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**3b**).

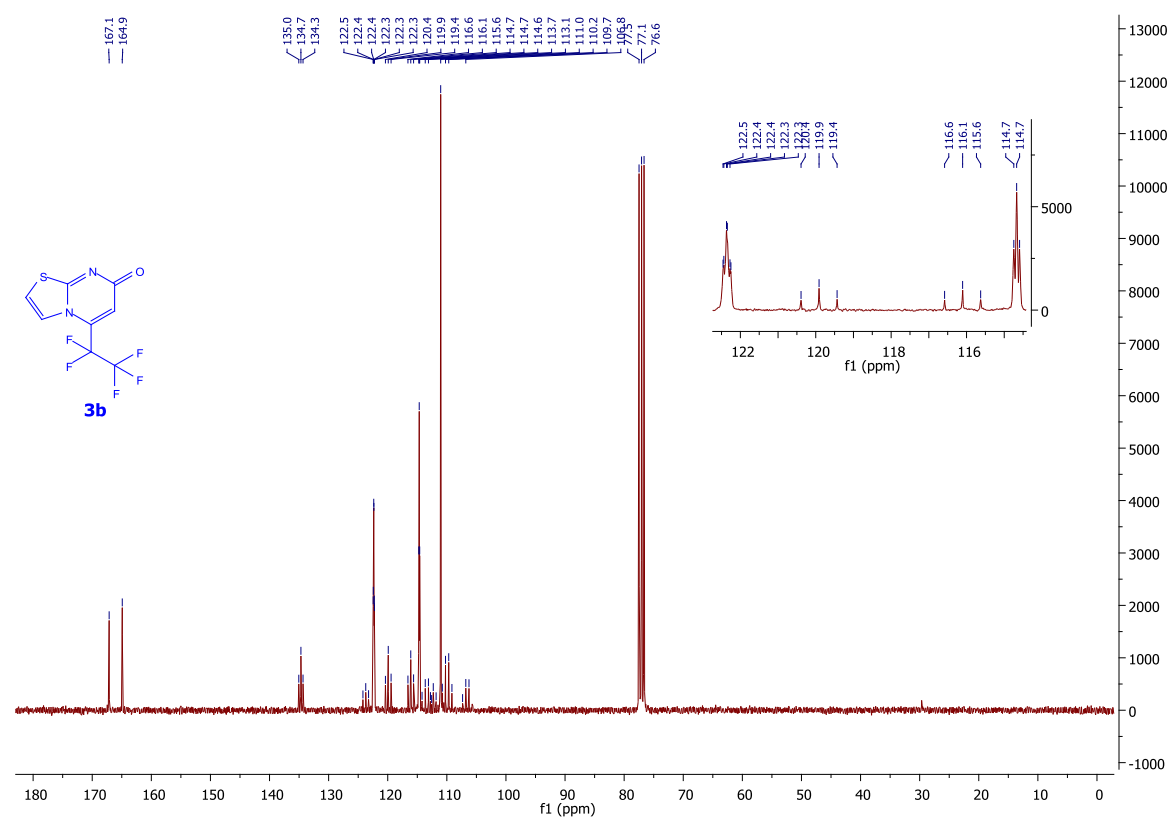
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

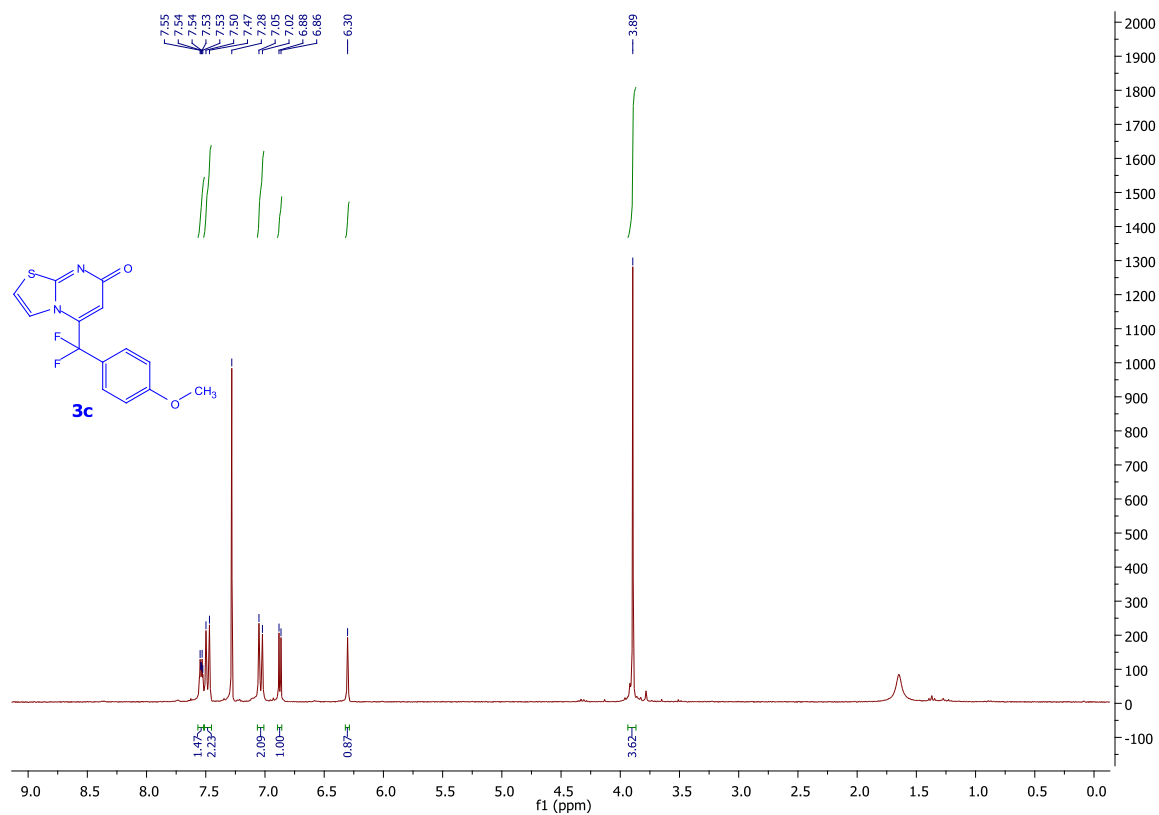


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

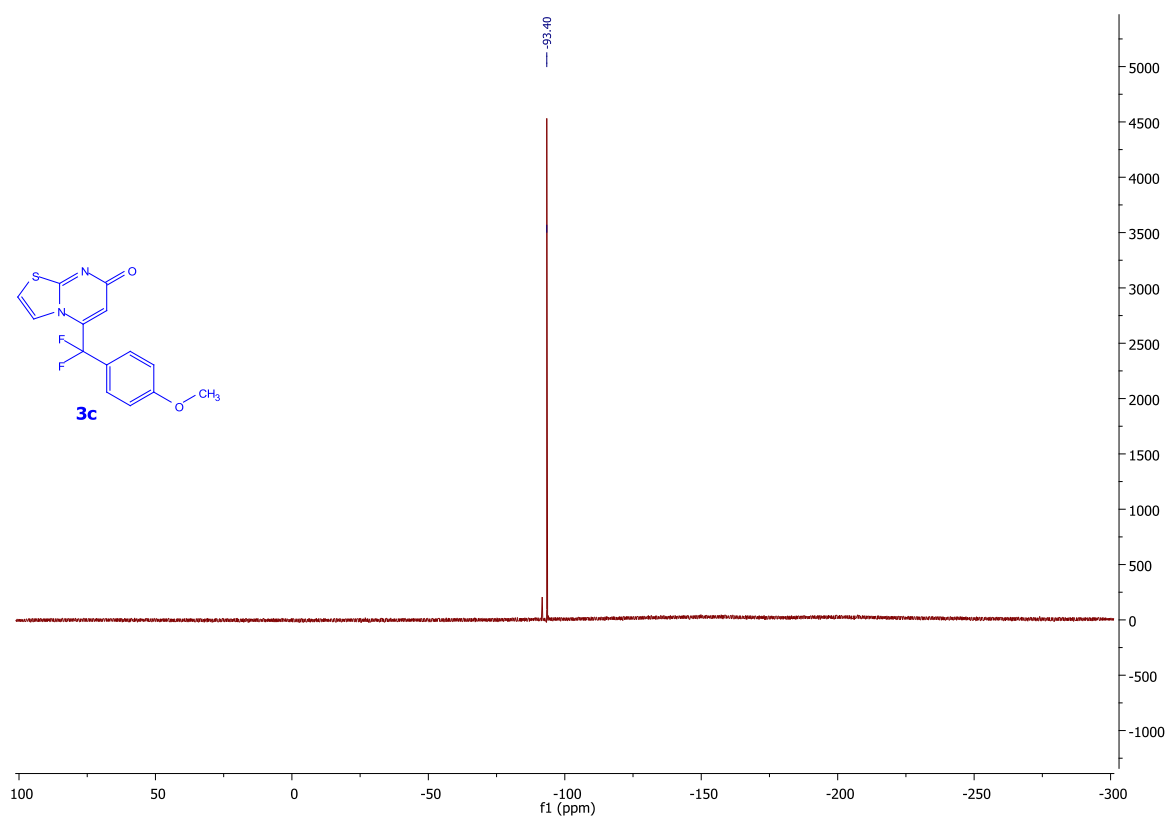


5-(difluoro(4-methoxyphenyl)methyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**3c**).

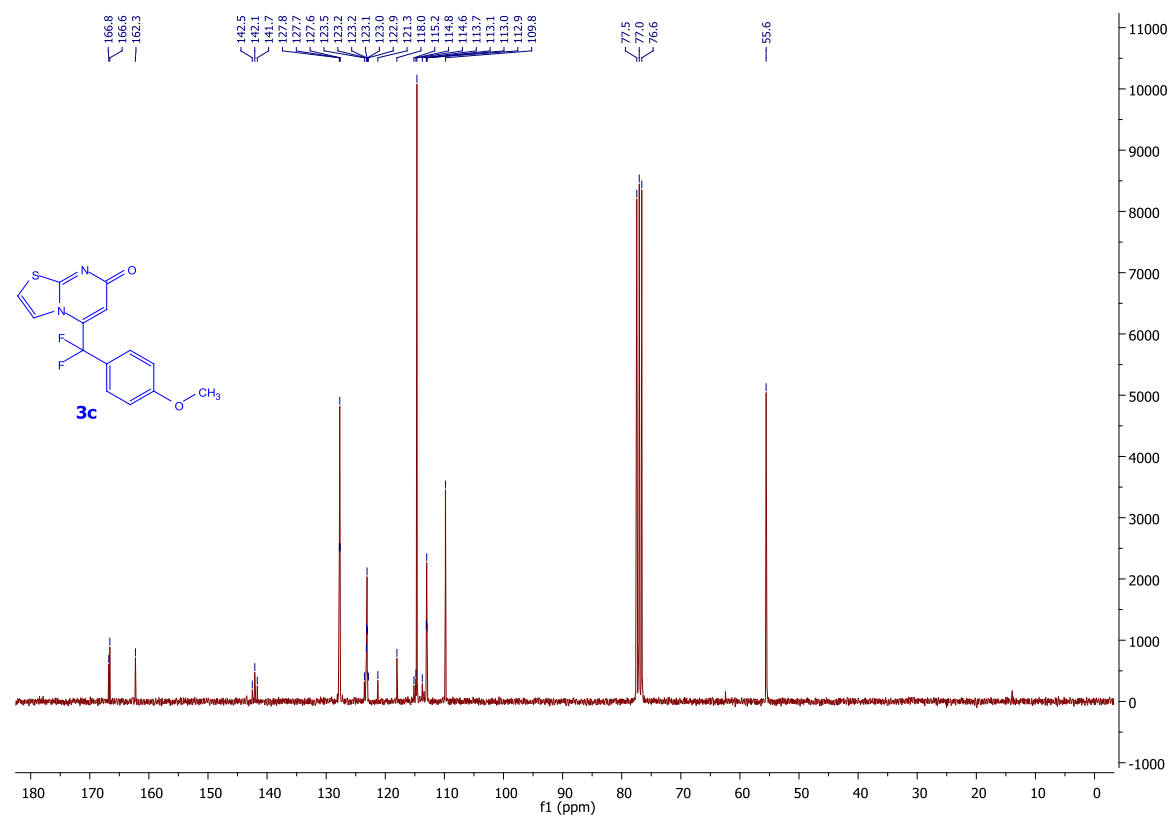
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

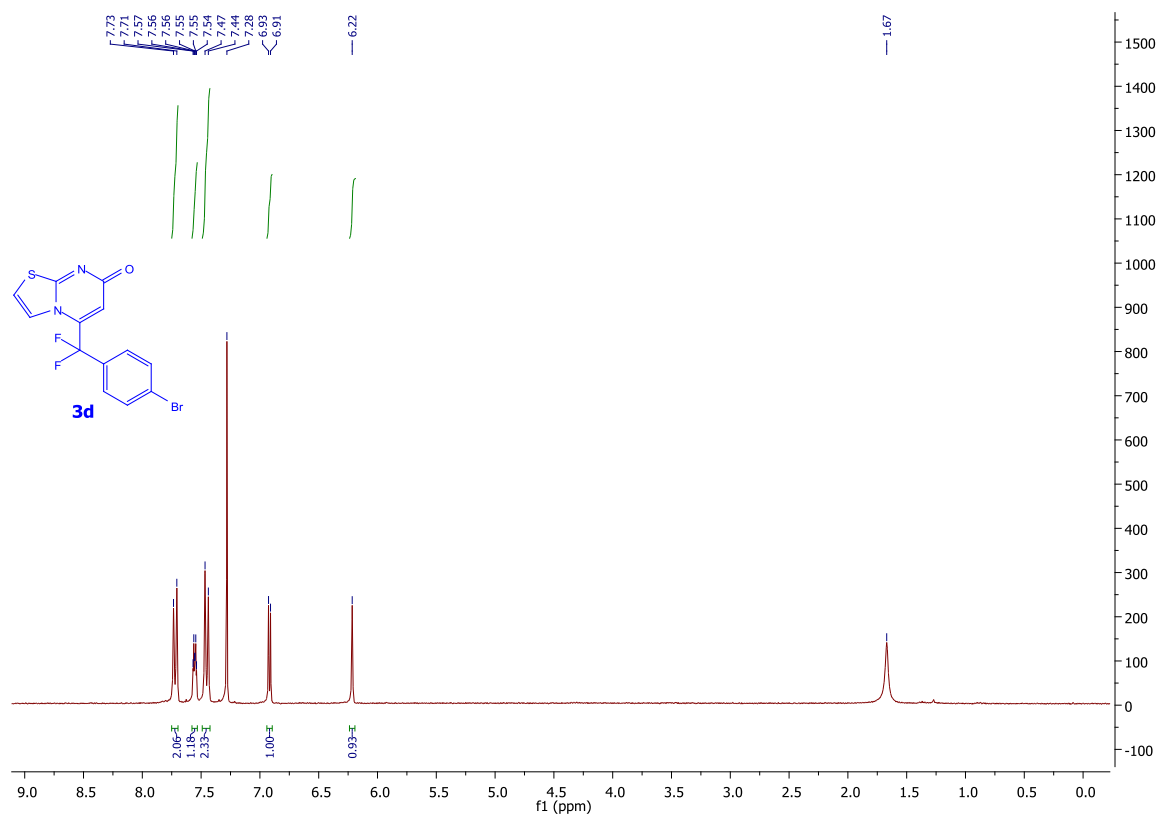


<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

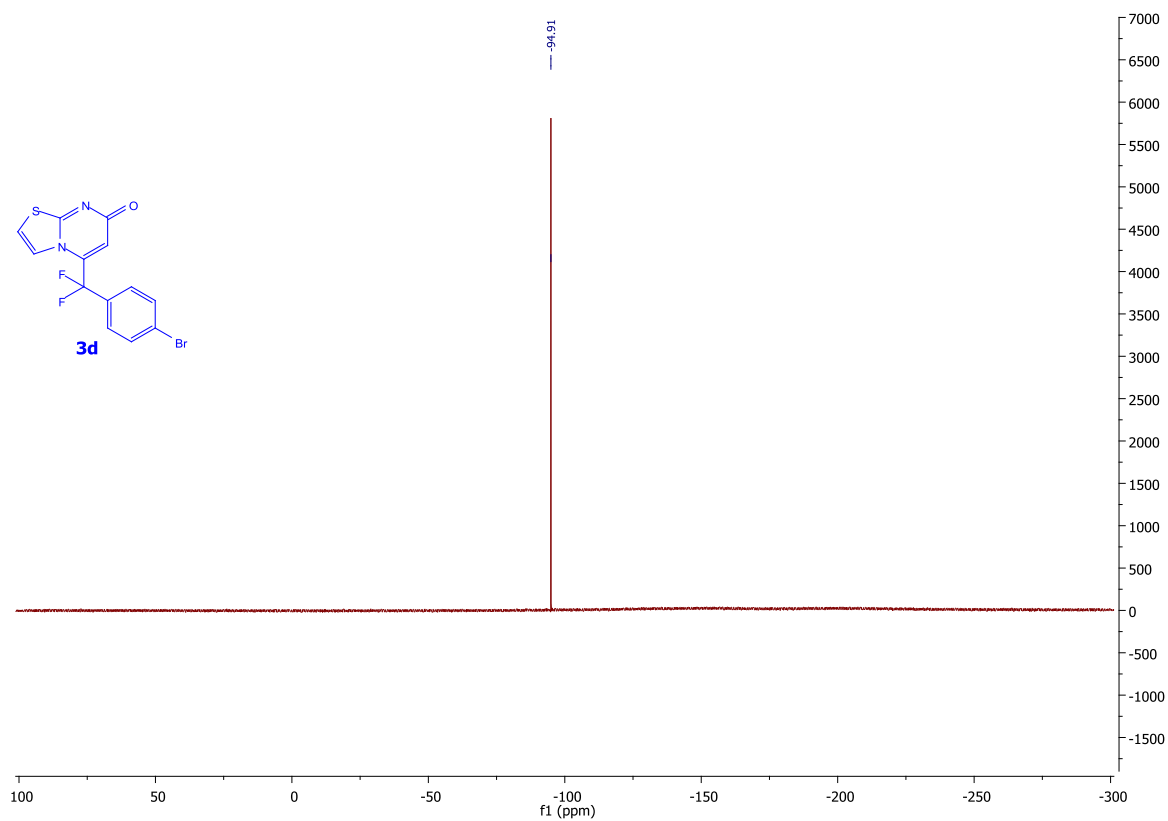


5-((4-bromophenyl)difluoromethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**3d**).

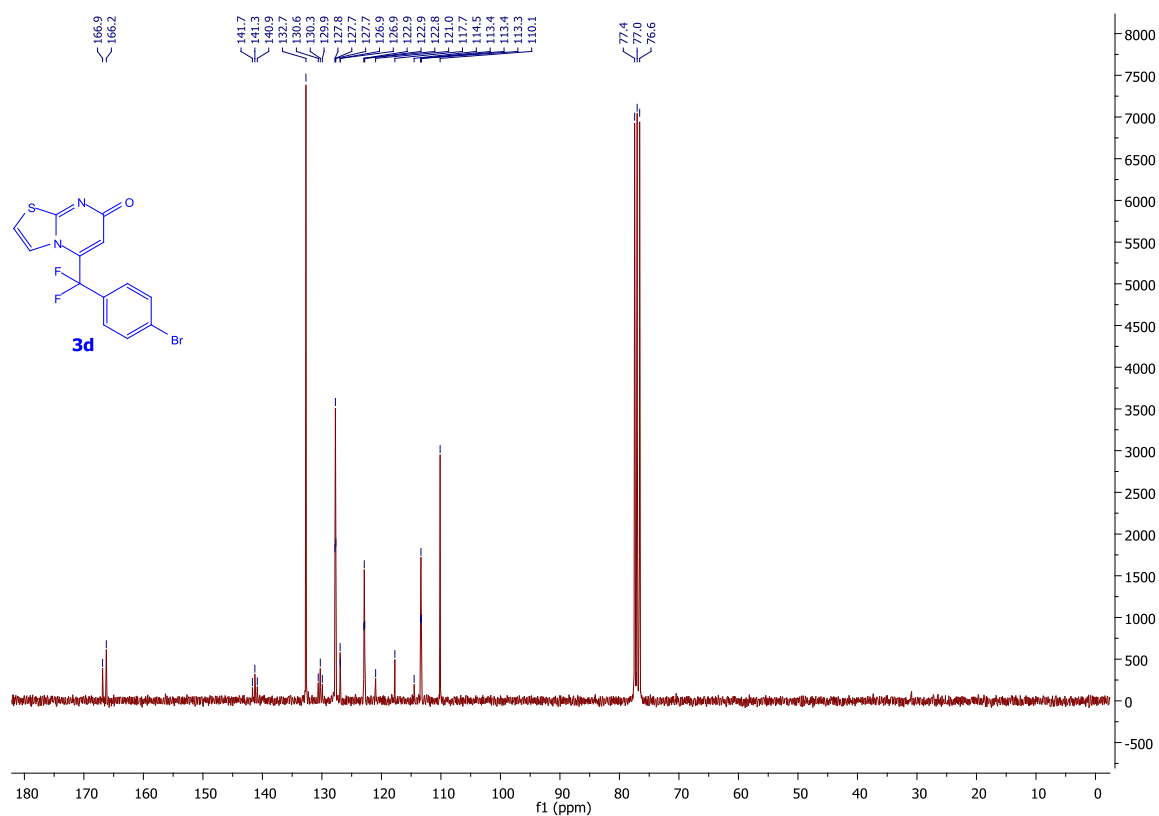
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



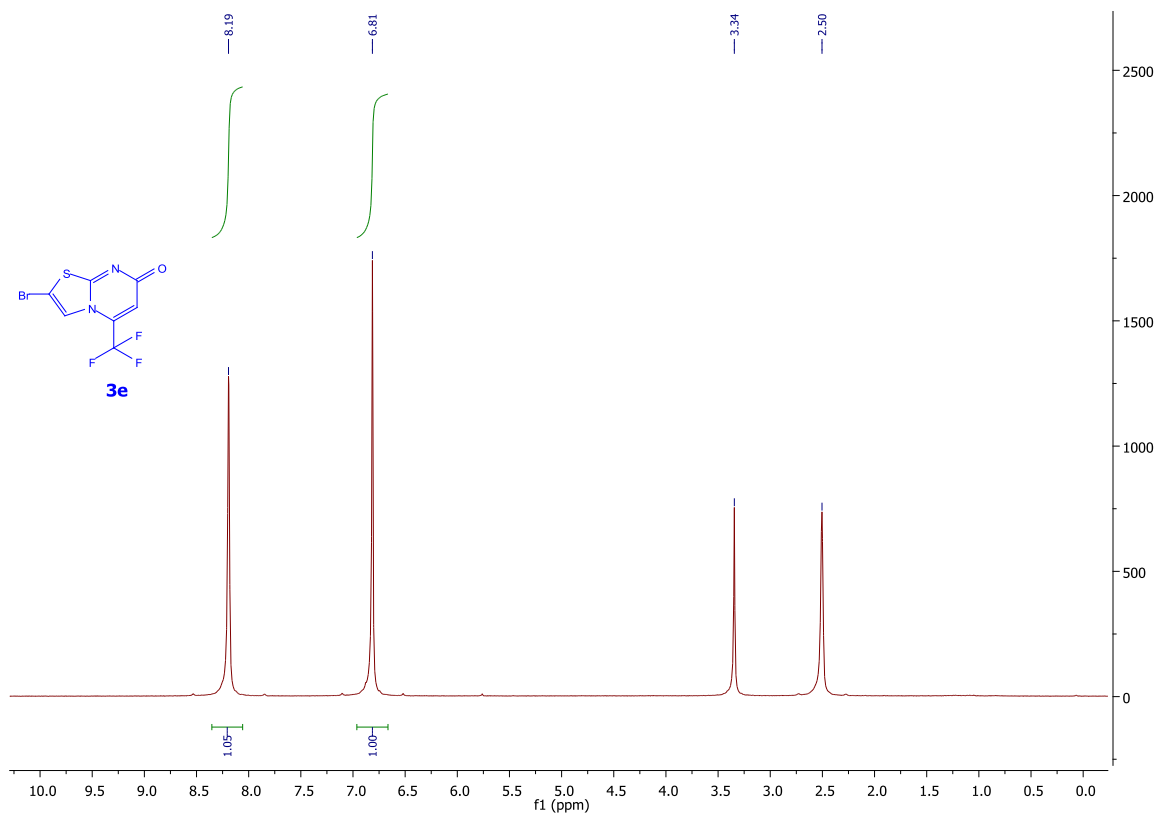
$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



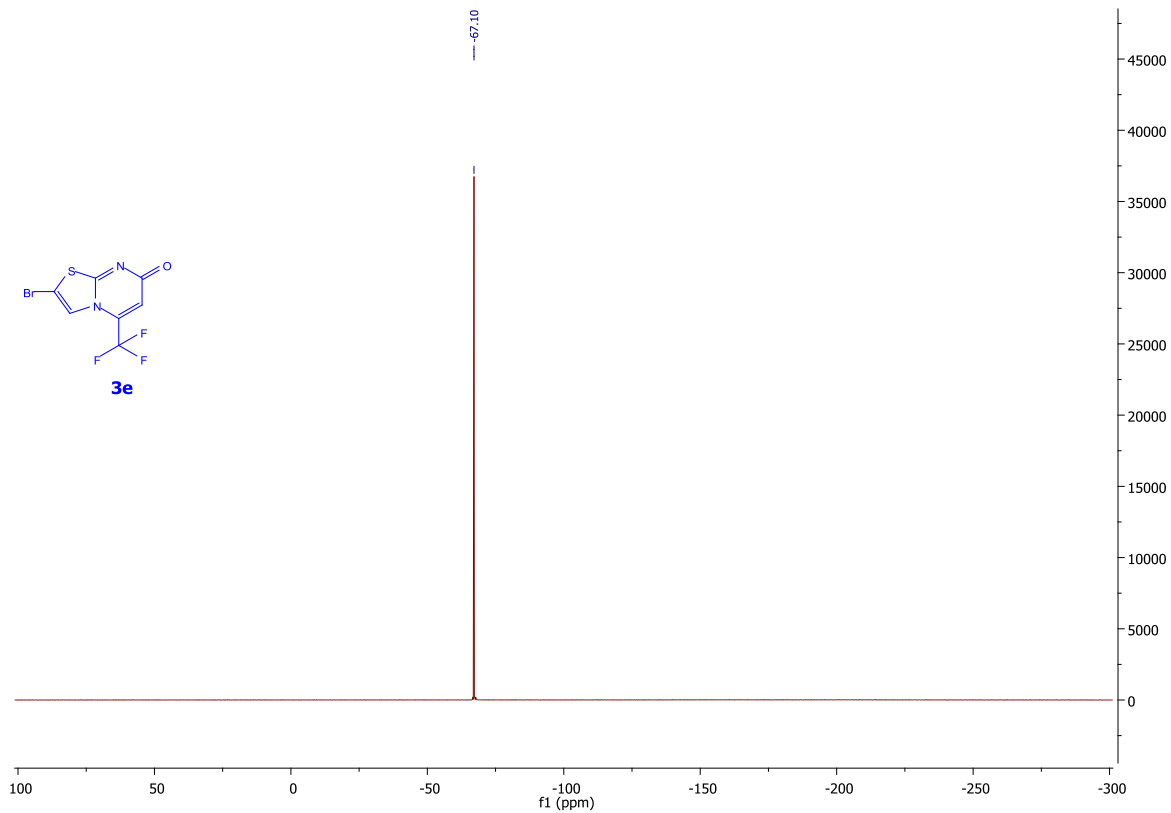
2-bromo-5-(trifluoromethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**3e**).

$^1\text{H}$  NMR (300 MHz,  $\text{DMSO}-d_6$ )

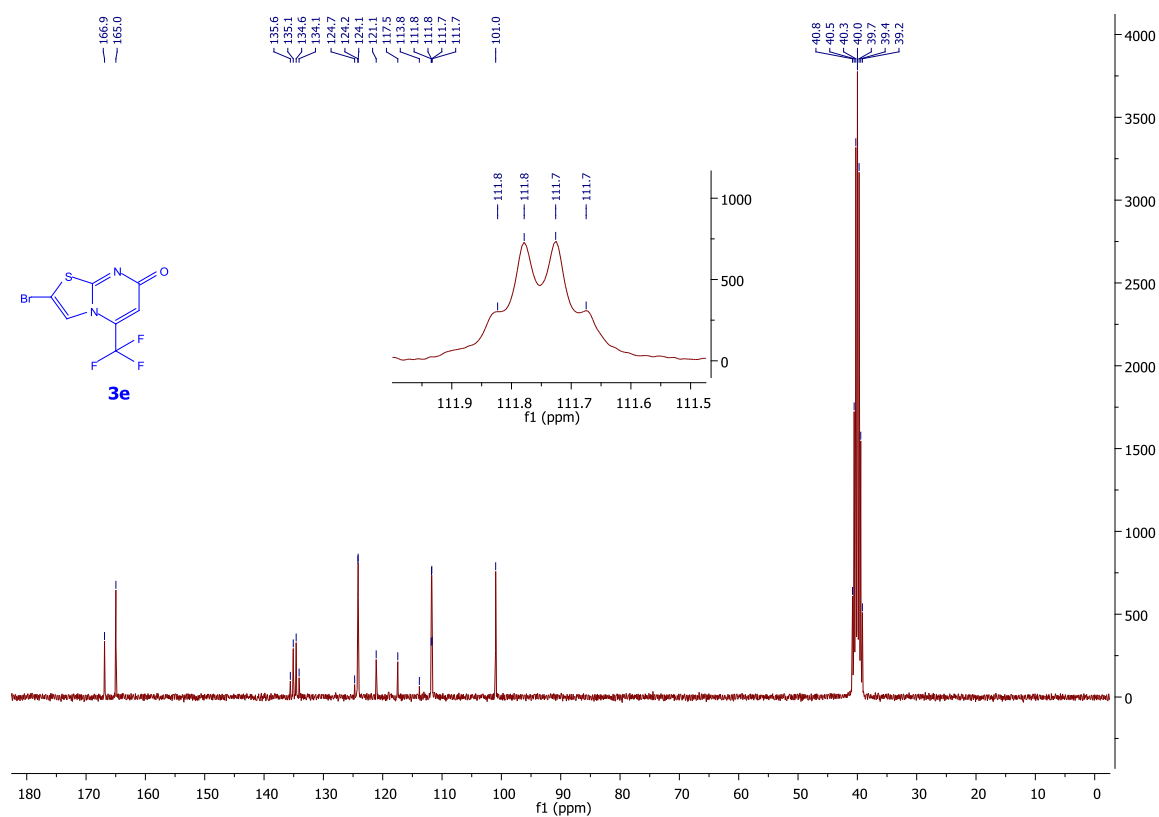




**<sup>19</sup>F NMR (282 MHz, DMSO-*d*<sub>6</sub>)**

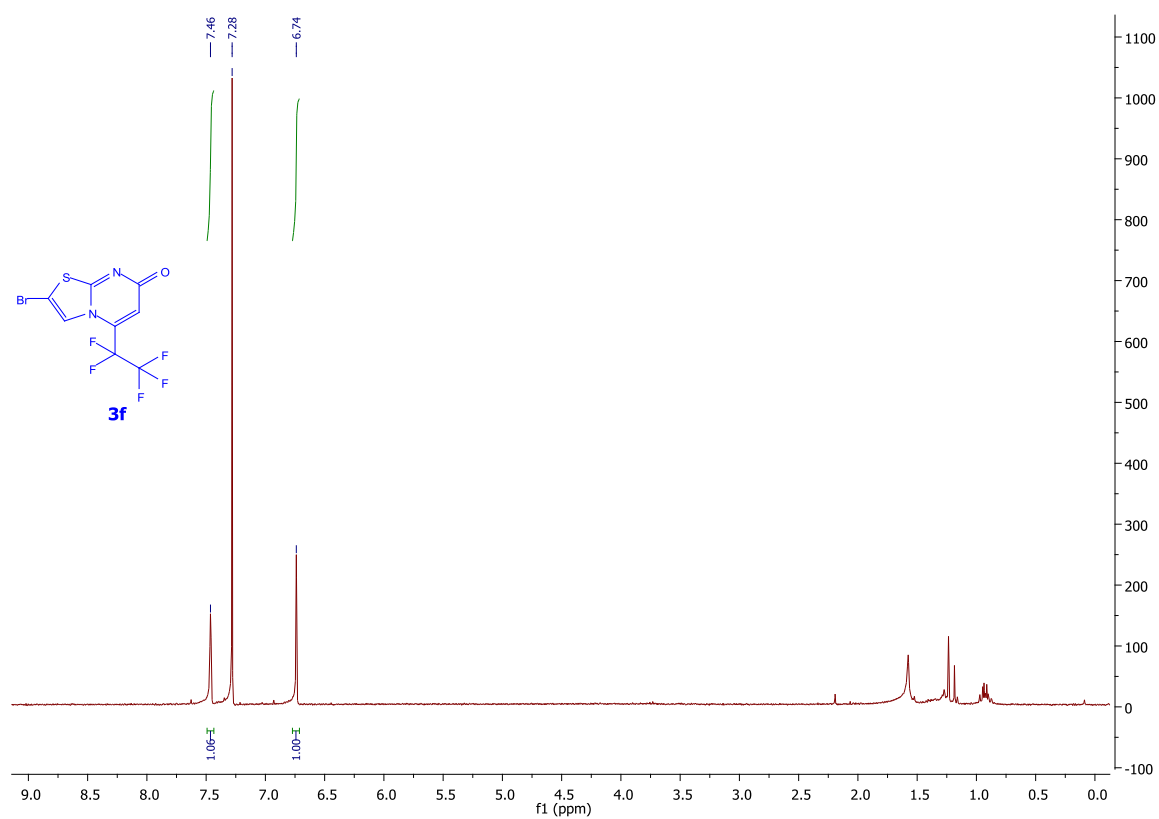


**<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)**

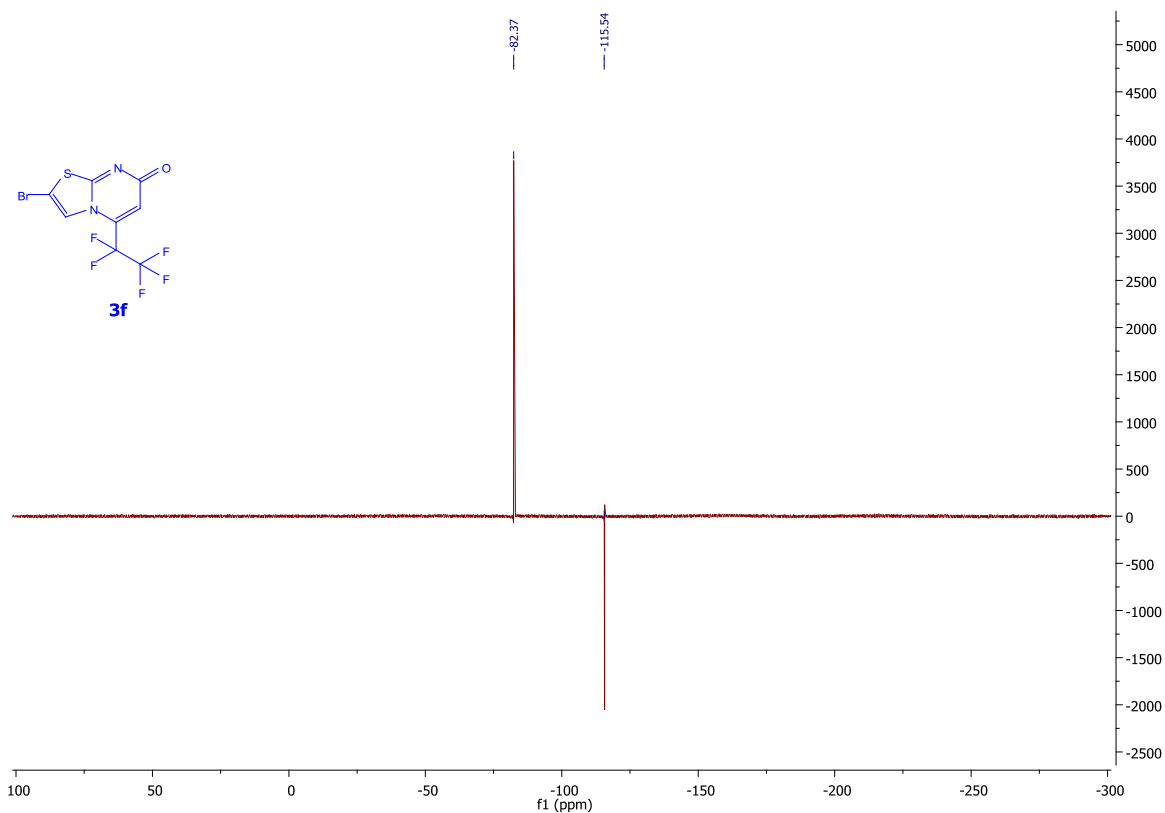


2-bromo-5-(perfluoroethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**3f**)

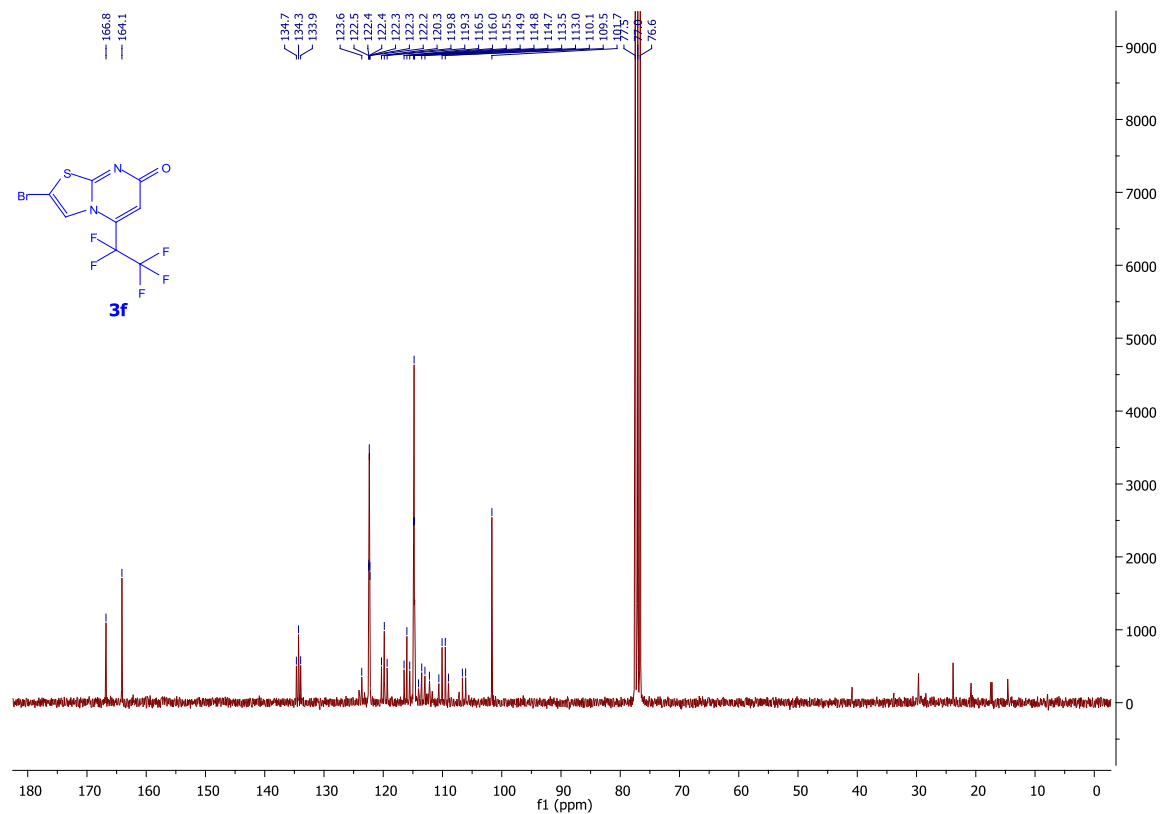
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

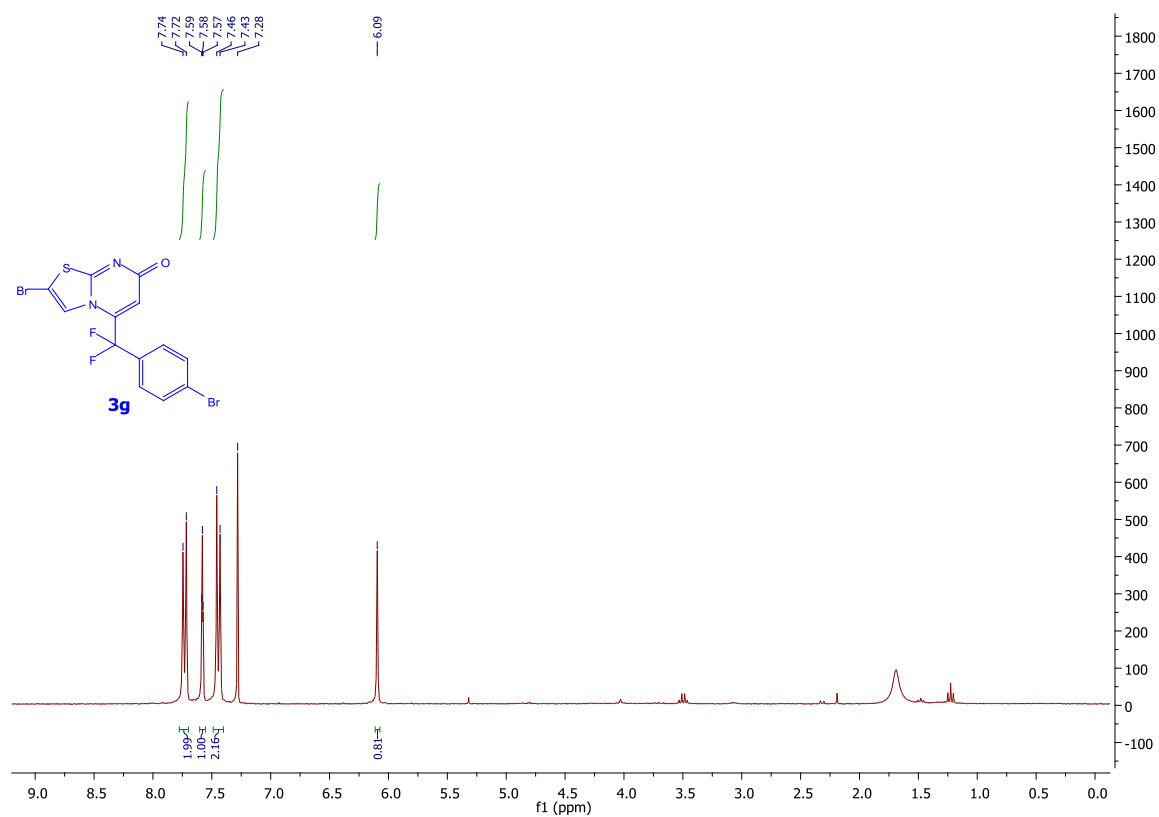


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

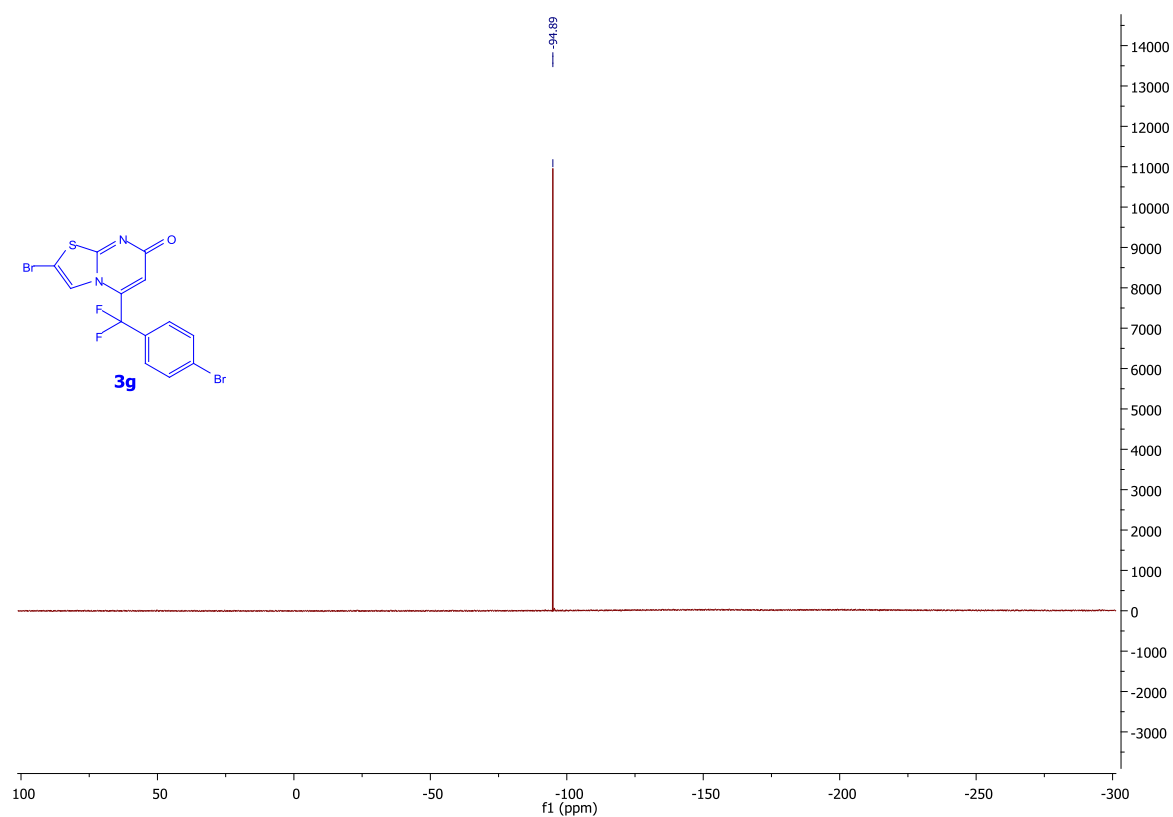


2-bromo-5-((4-bromophenyl)difluoromethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**3g**).

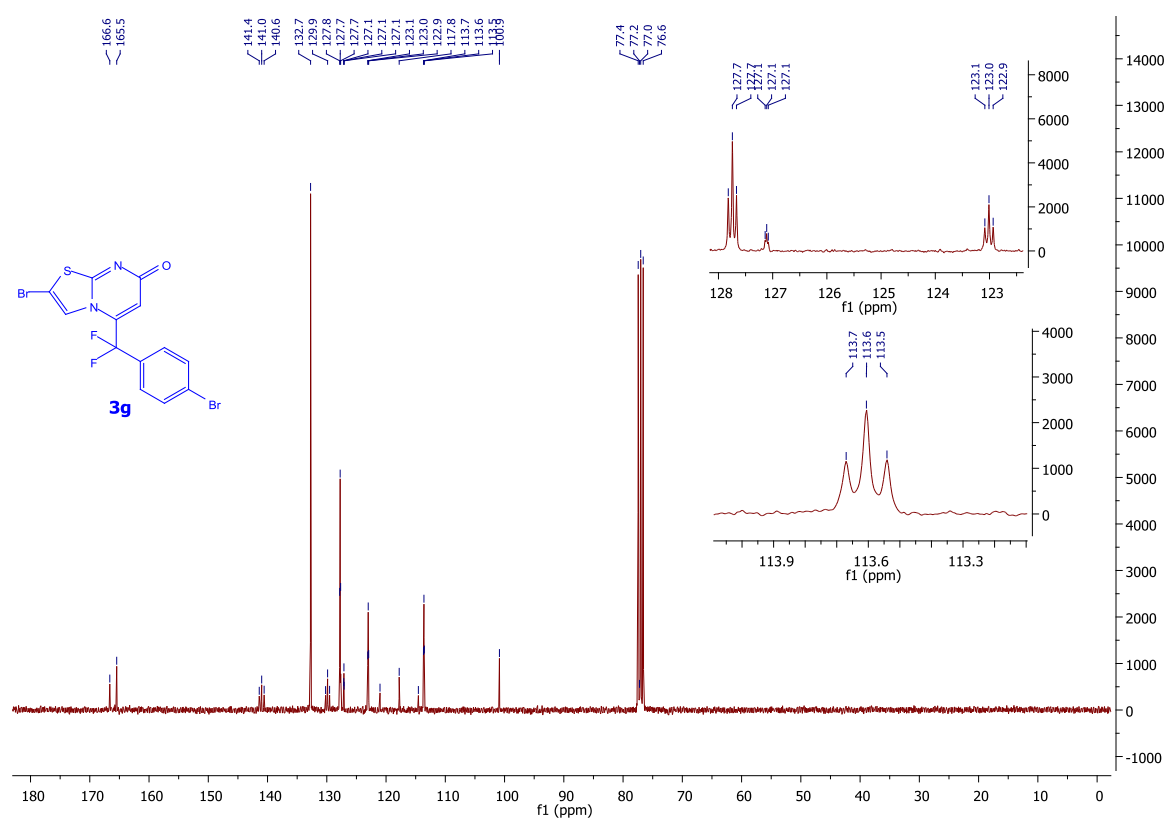
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

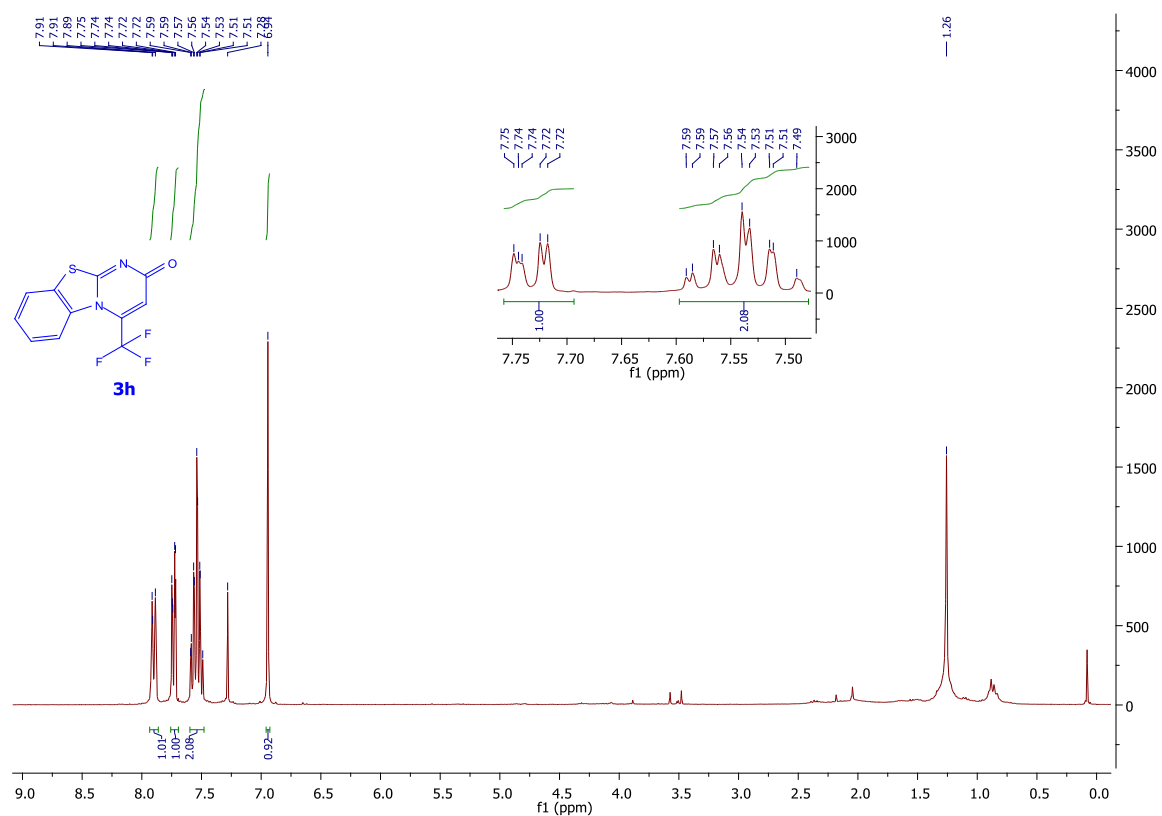


<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

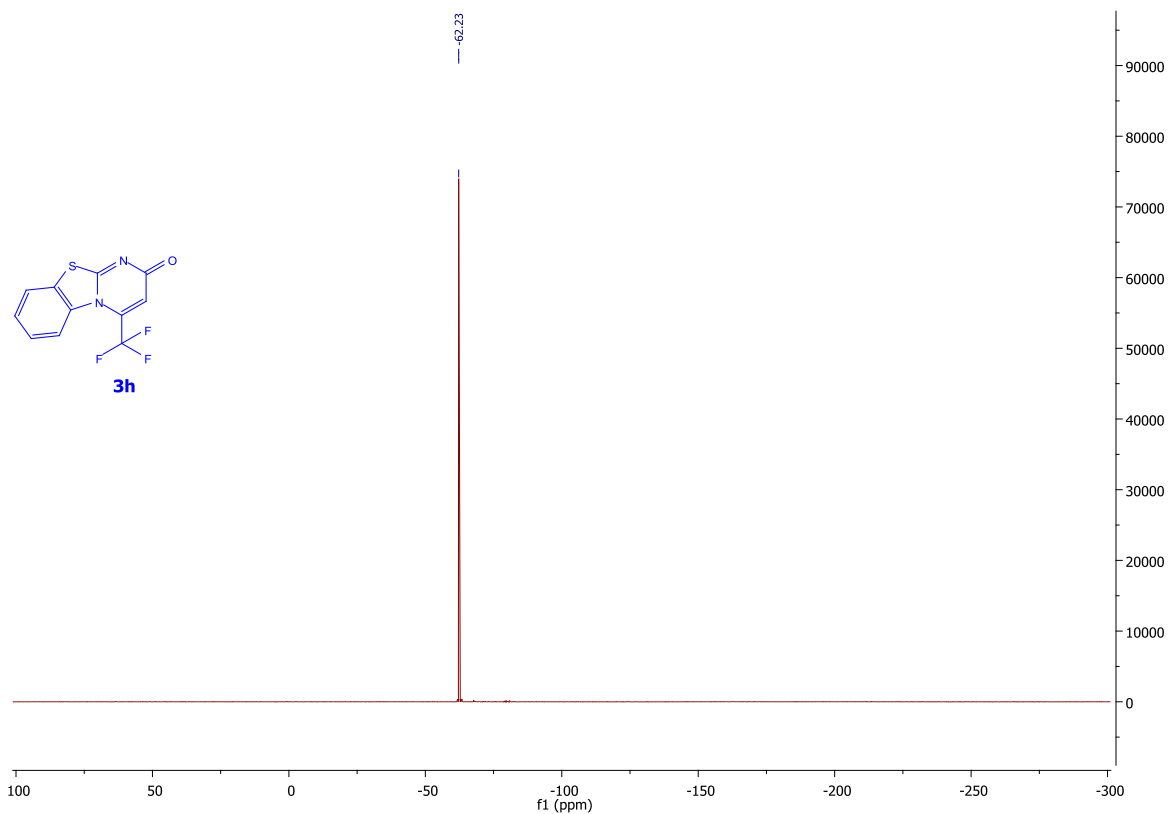


4-(trifluoromethyl)-2H-benzo[4,5]thiazolo[3,2-a]pyrimidin-2-one (**3h**).

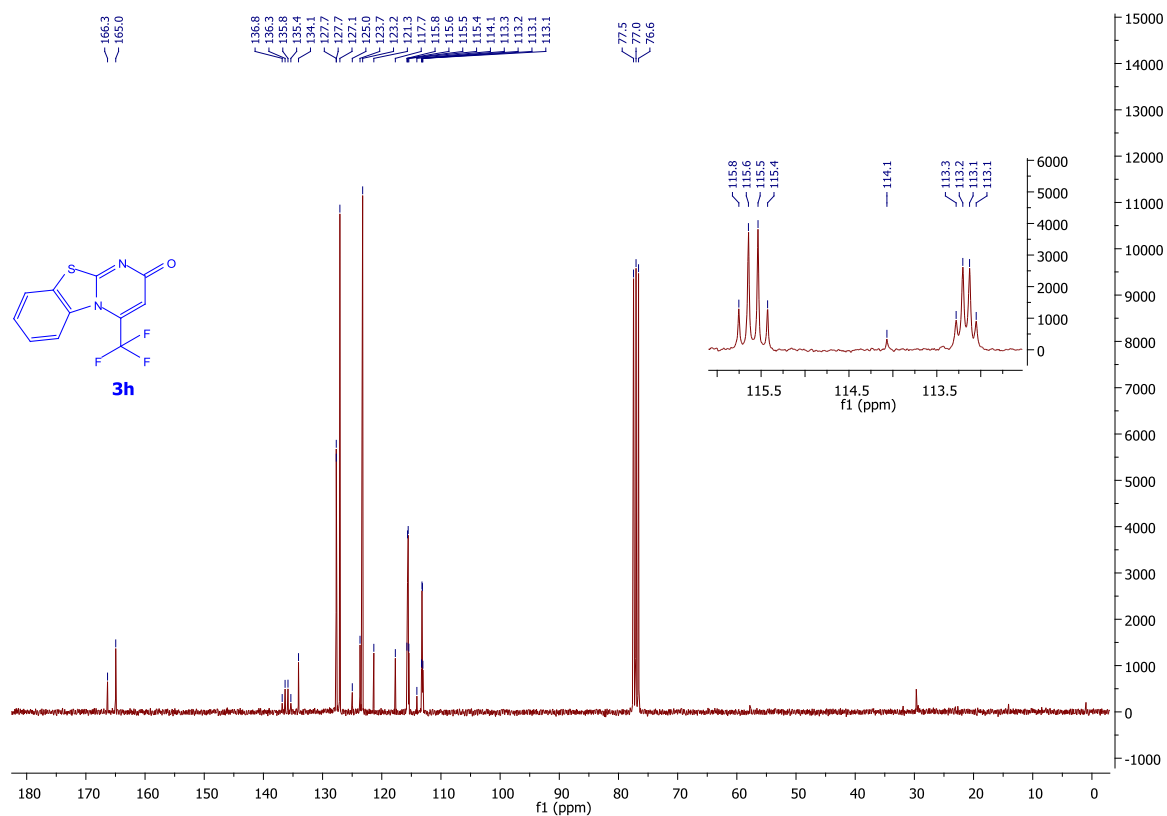
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

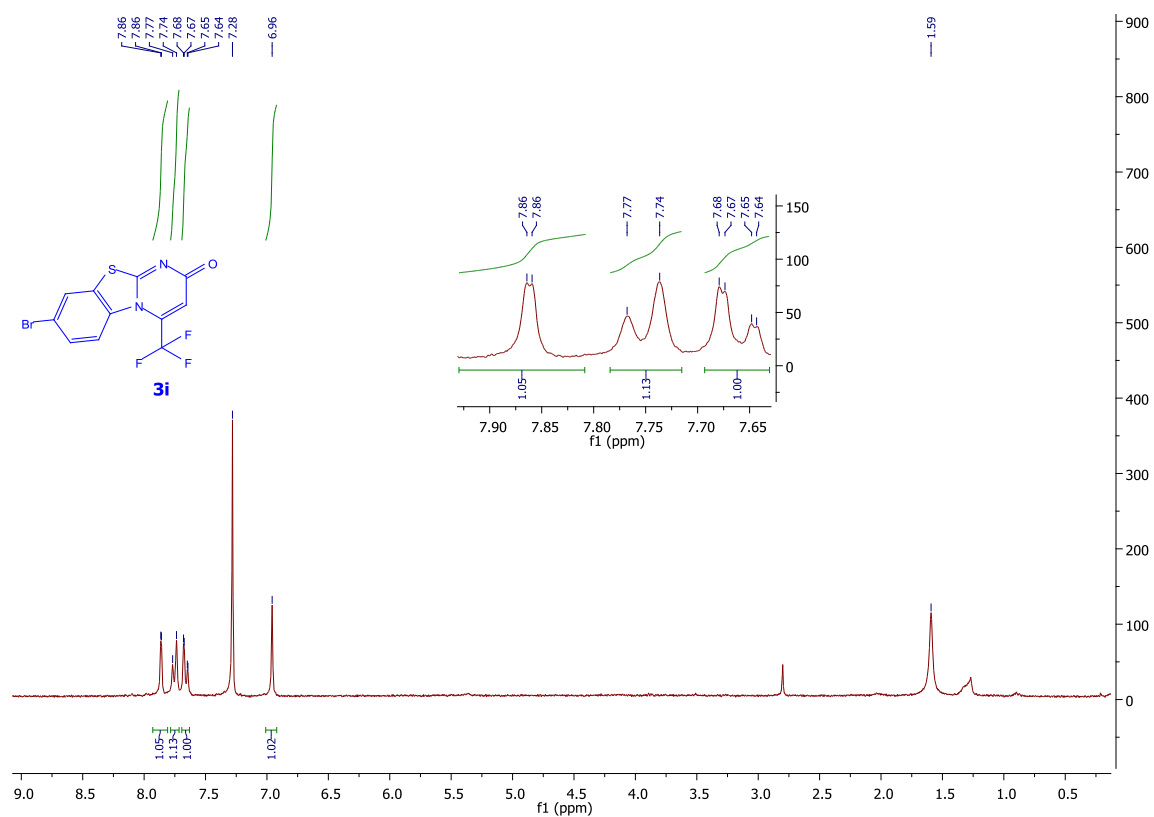


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

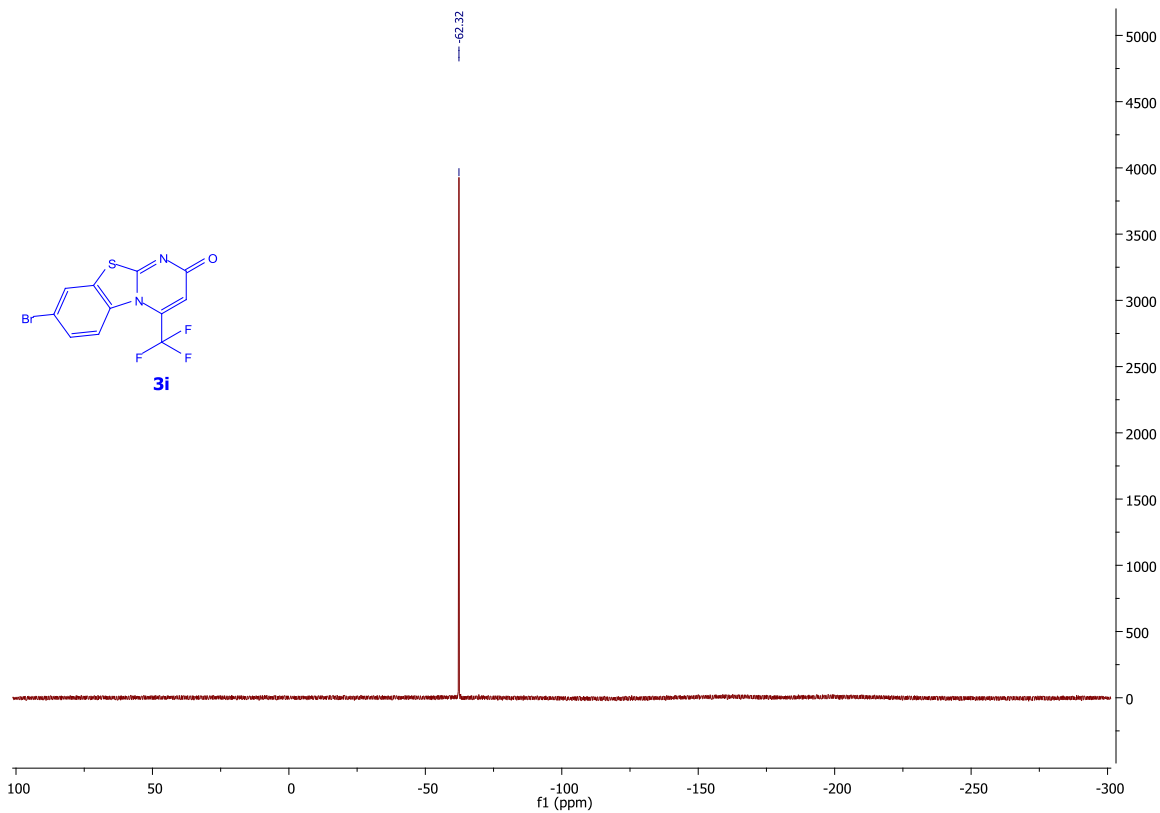


*8-bromo-4-(trifluoromethyl)-2H-benzo[4,5]thiazolo[3,2-*a*]pyrimidin-2-one (3i).*

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

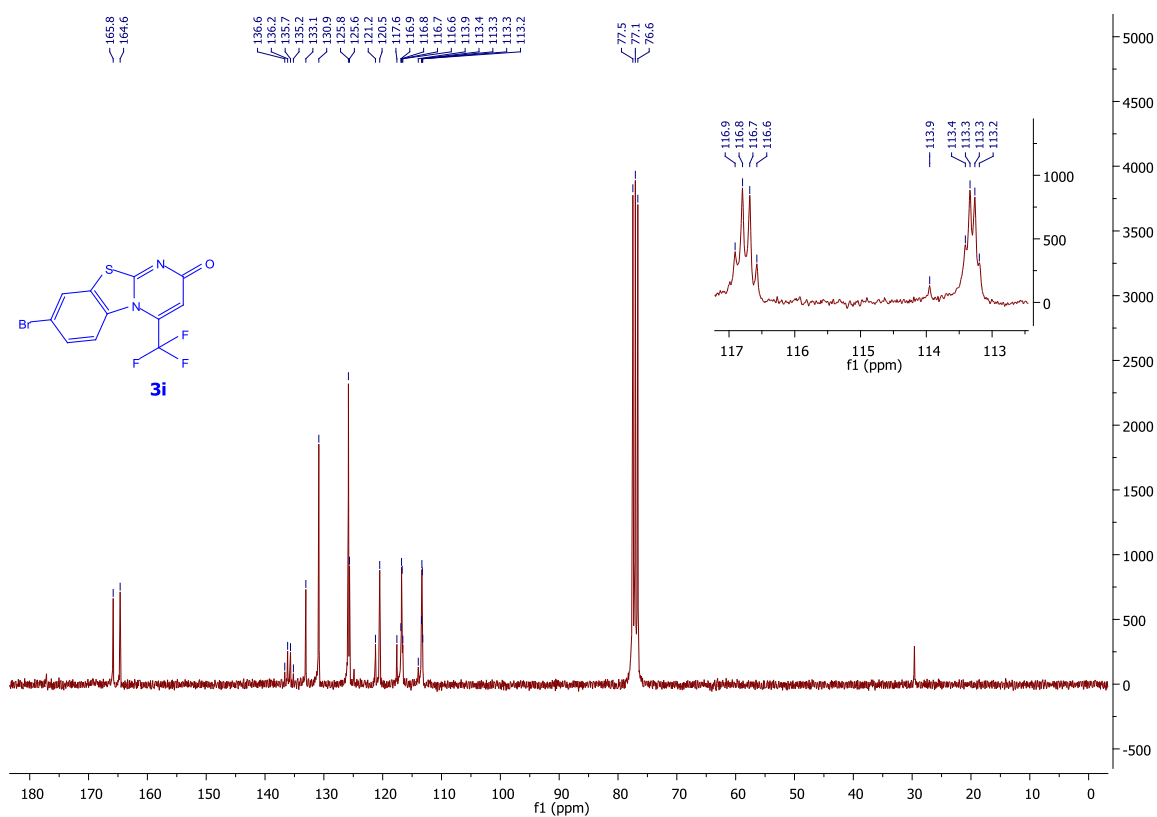


**<sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>)**



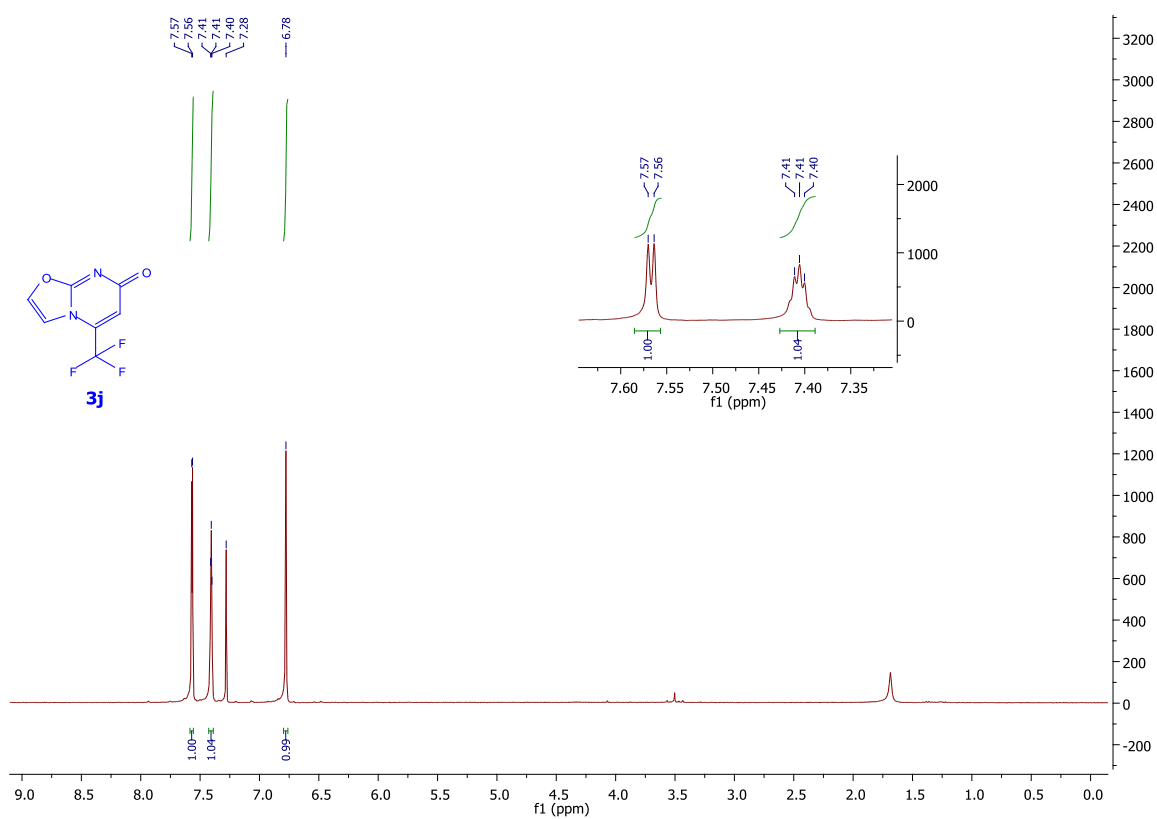
**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)**



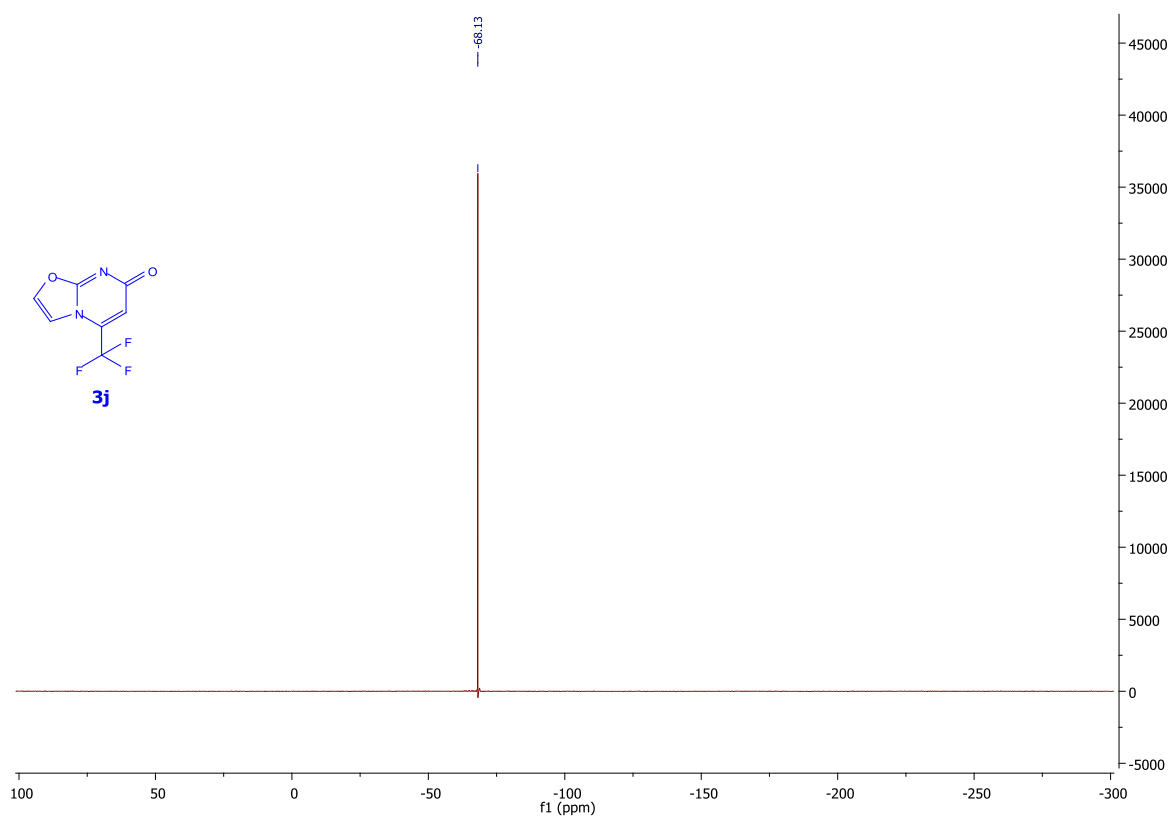


5-(trifluoromethyl)-7H-oxazolo[3,2-a]pyrimidin-7-one (**3j**)

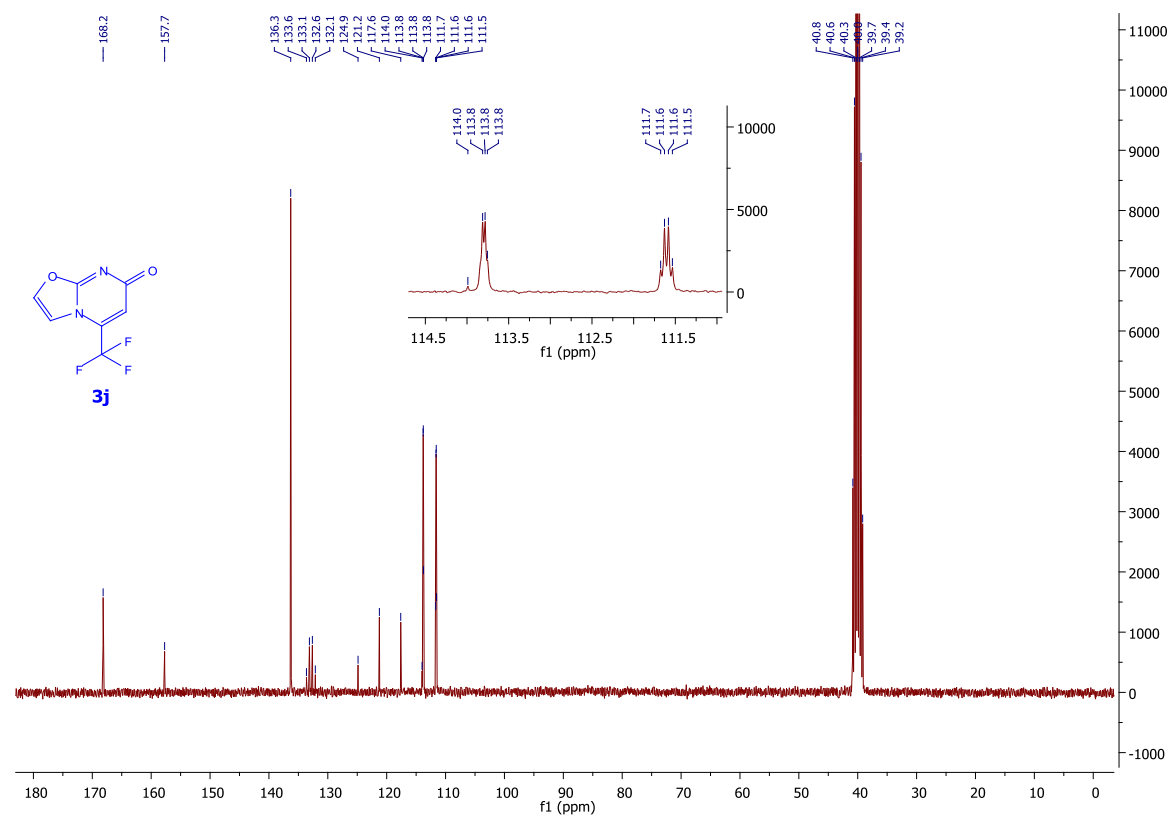
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

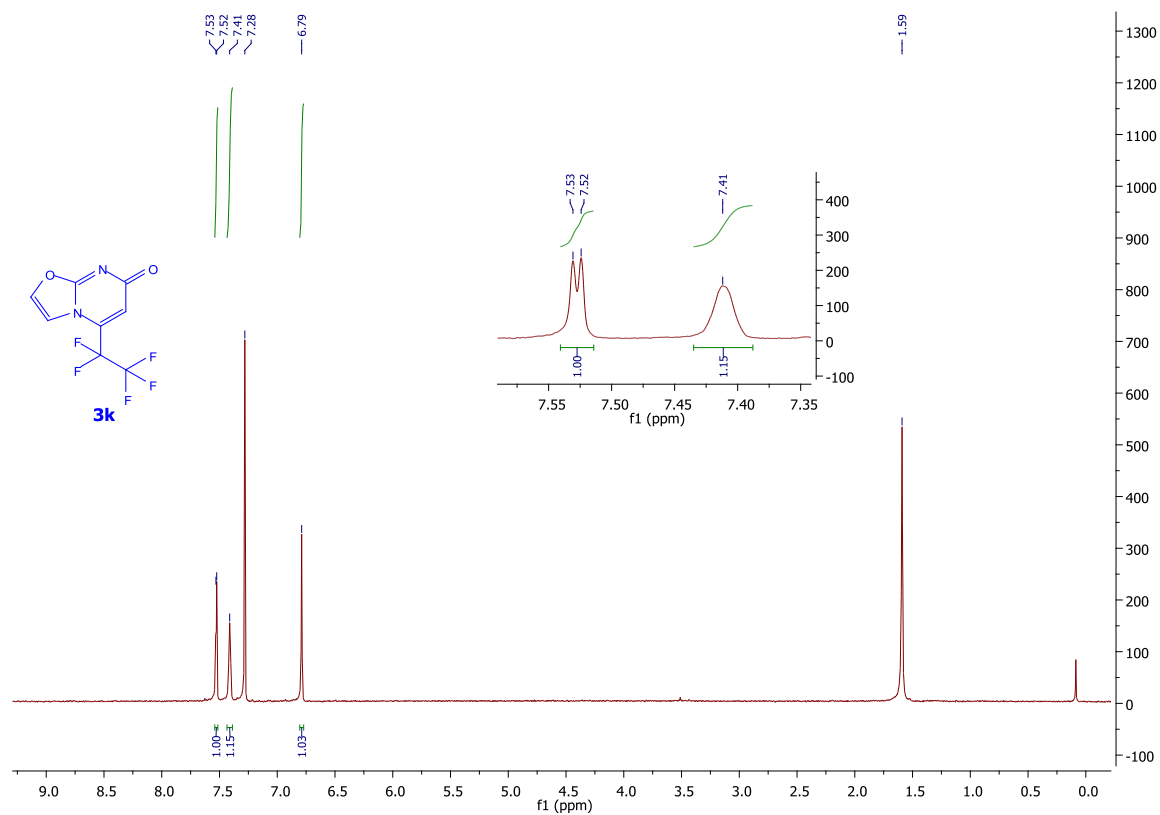


$^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ )

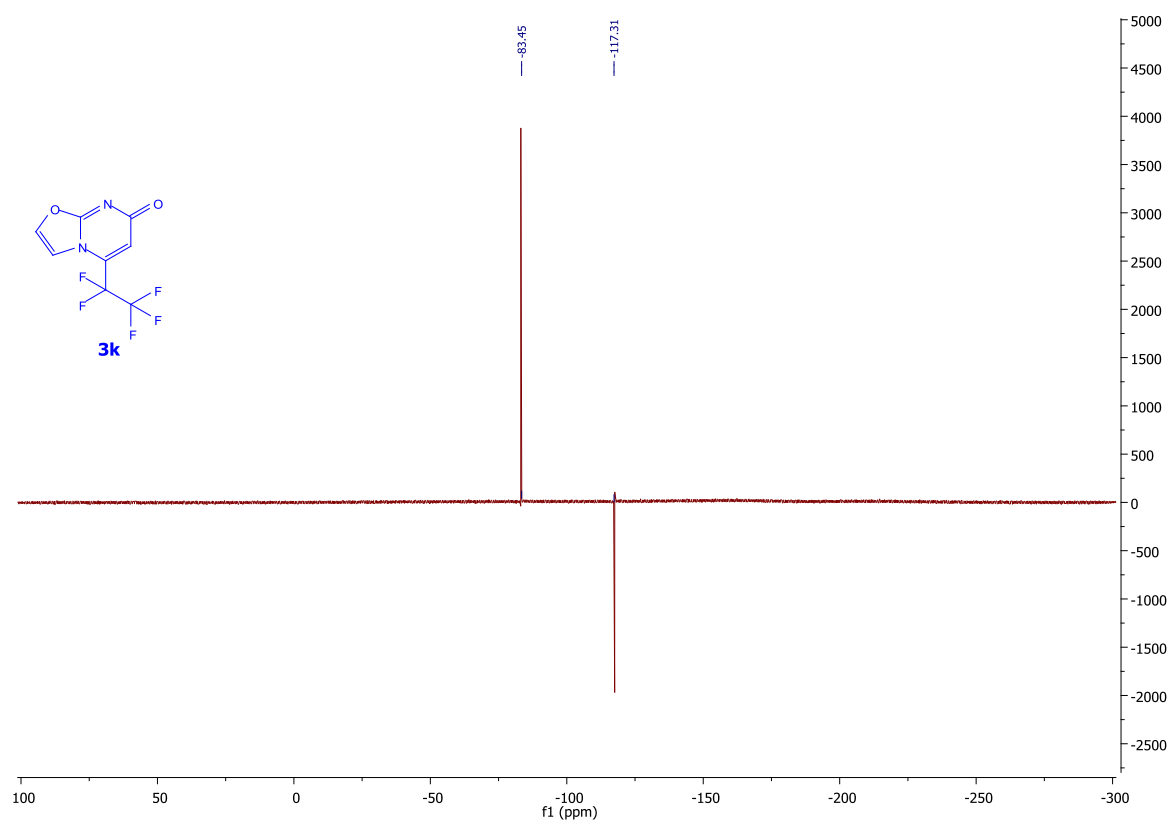


5-(perfluoroethyl)-7H-oxazolo[3,2-a]pyrimidin-7-one (**3k**)

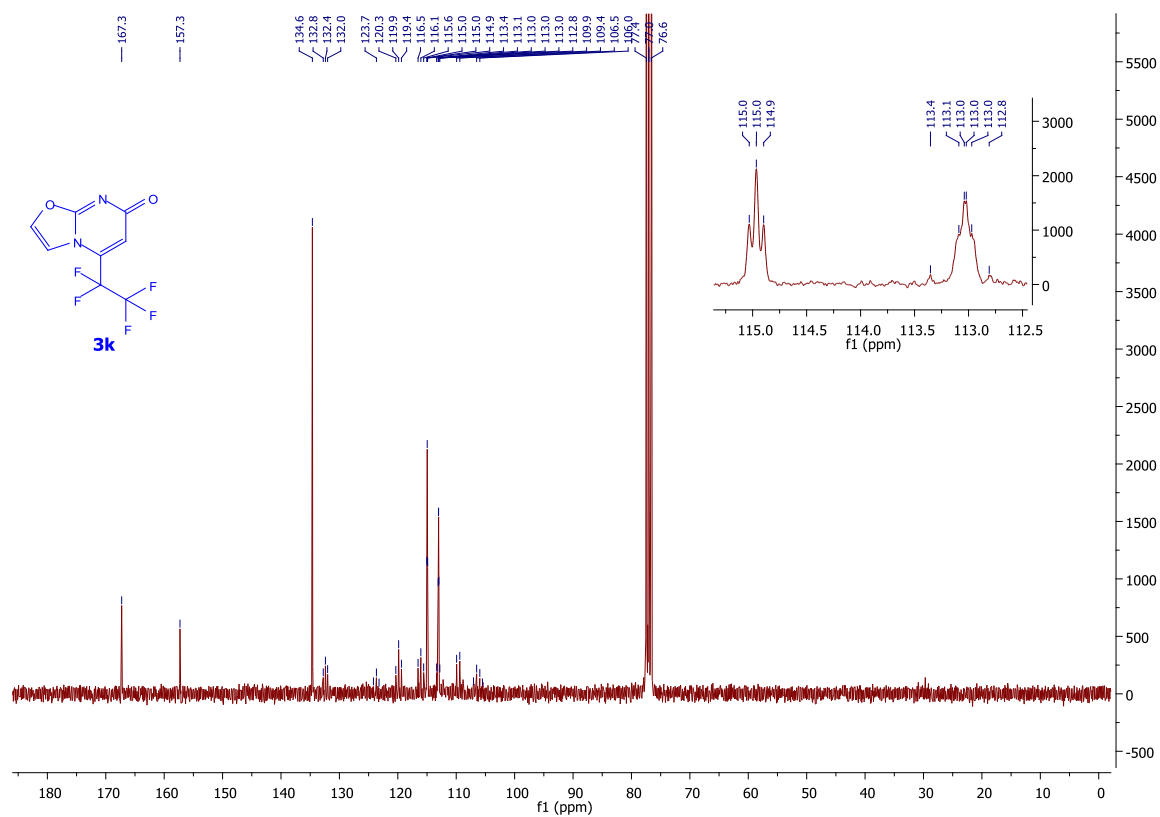
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

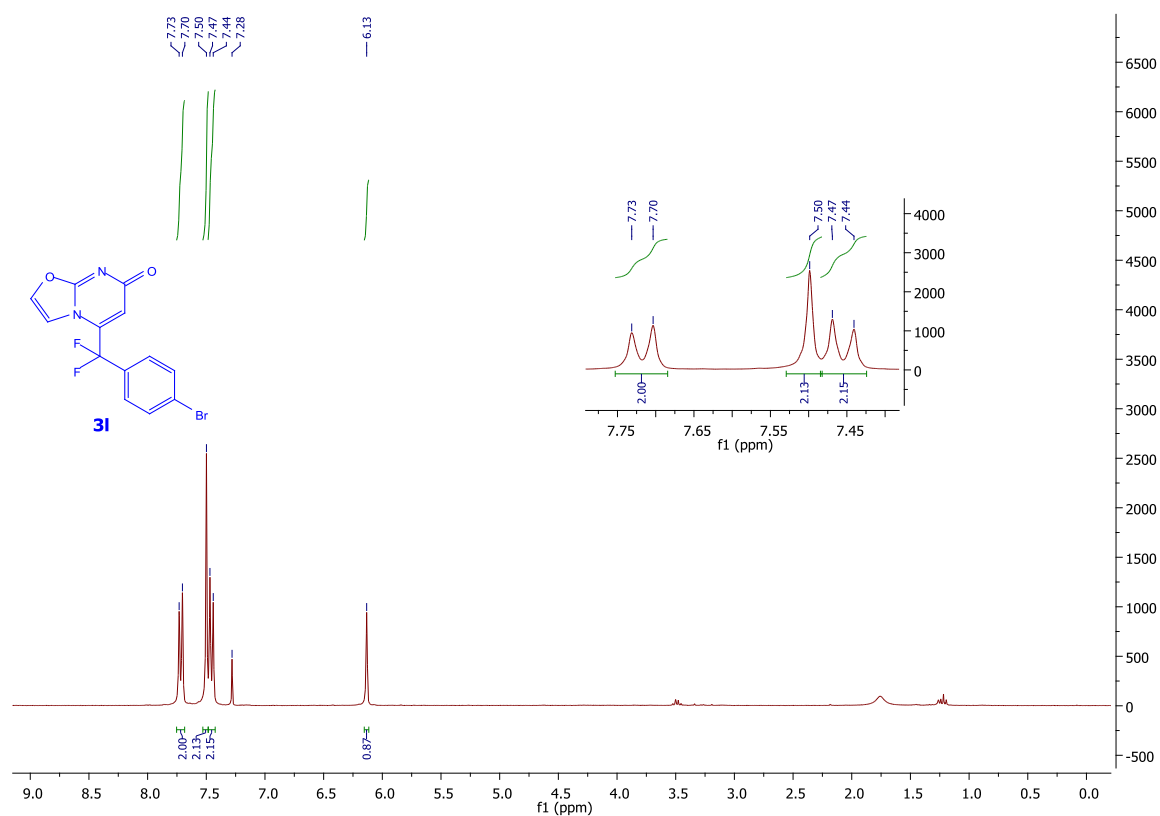


<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

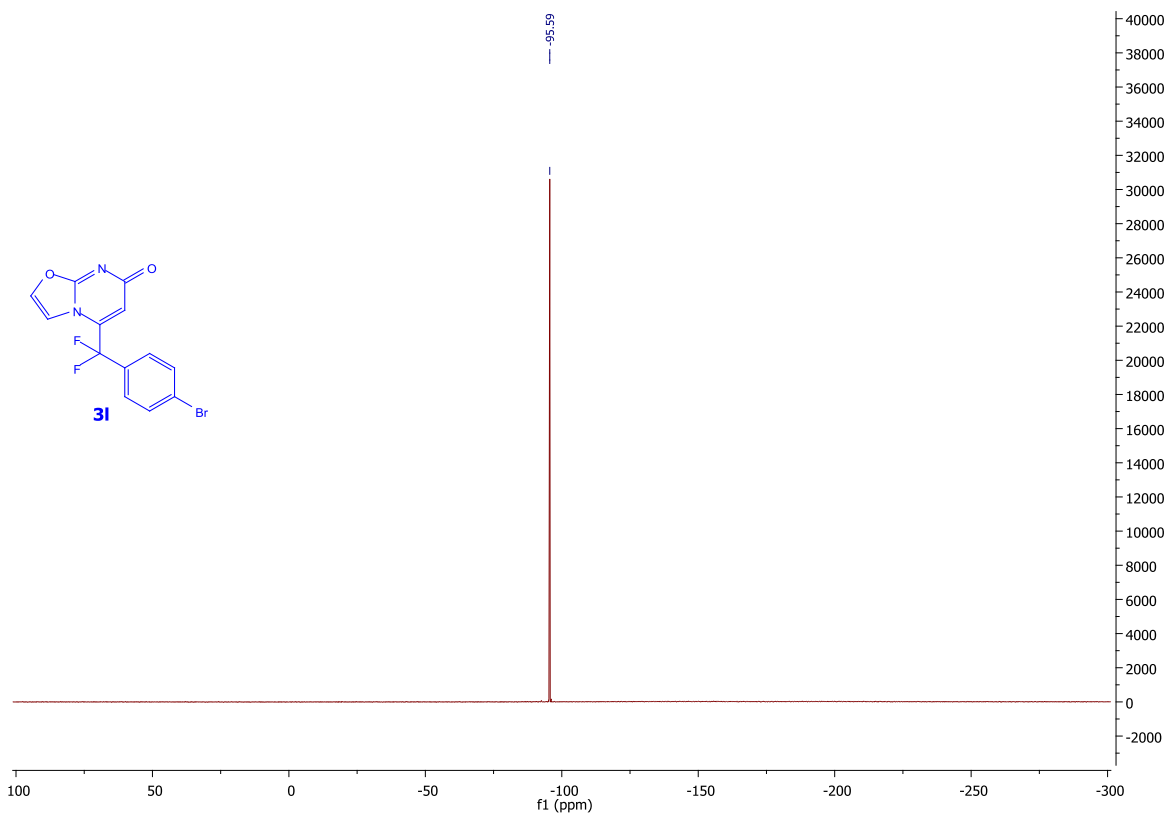


5-((4-bromophenyl)difluoromethyl)-7H-oxazolo[3,2-a]pyrimidin-7-one (**3l**)

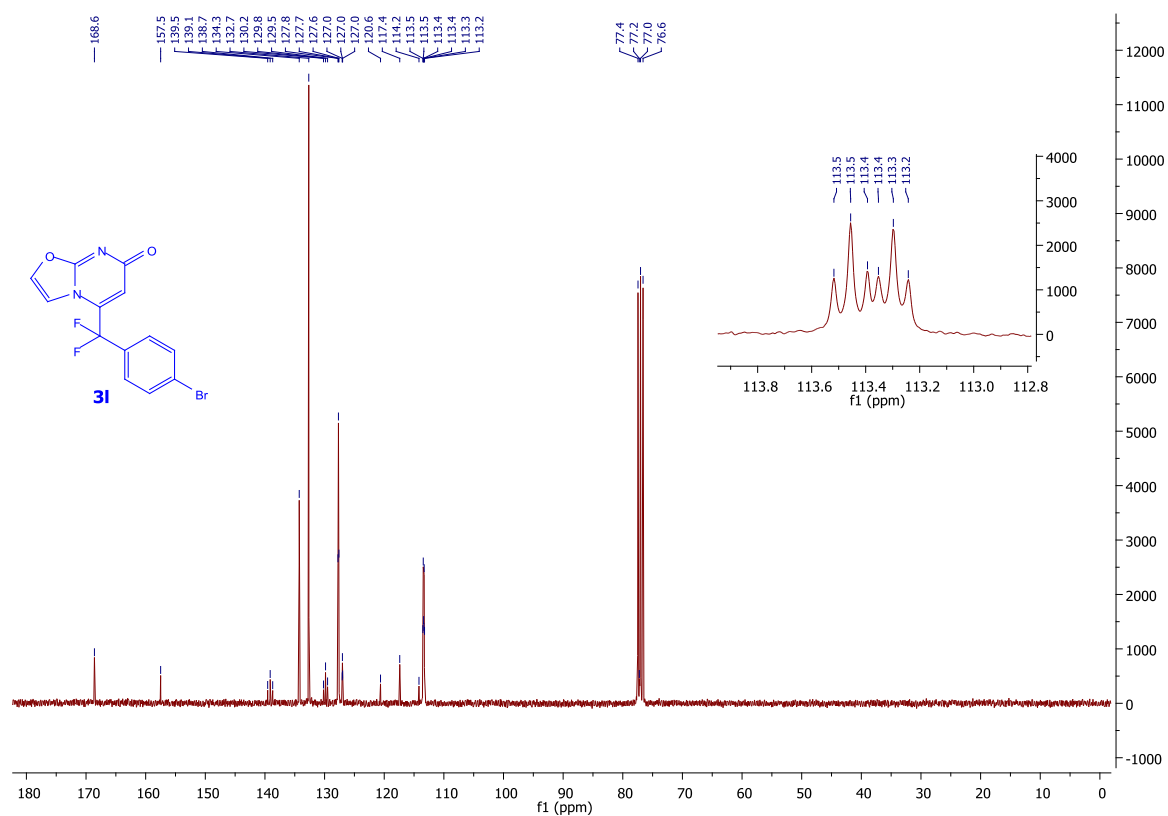
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

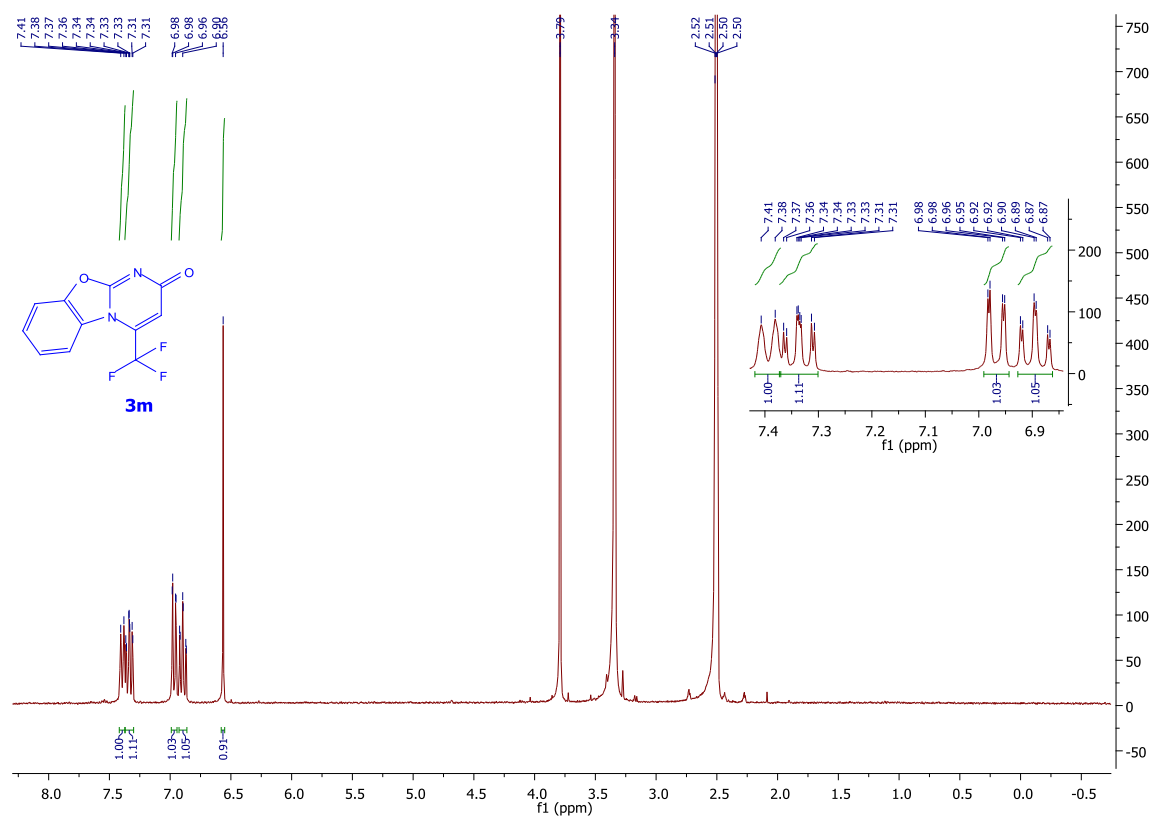


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

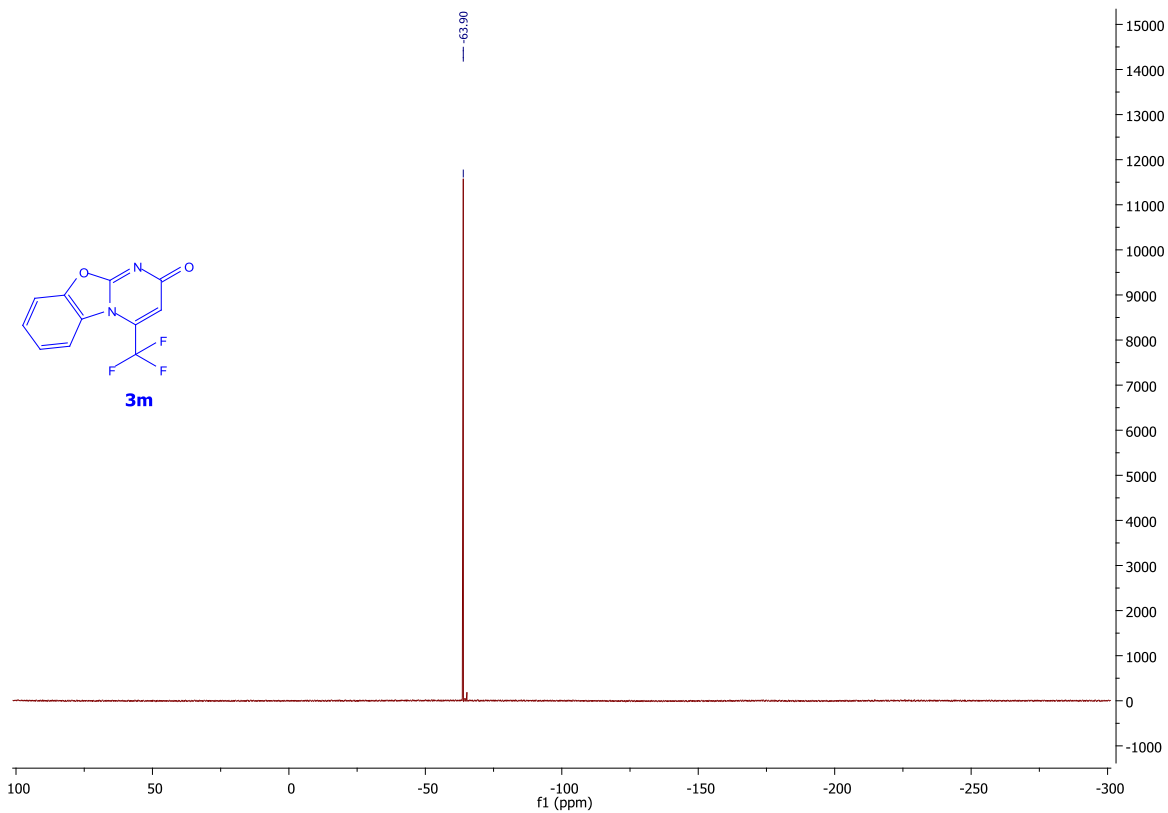


4-(trifluoromethyl)-2H-benzo[4,5]oxazolo[3,2-a]pyrimidin-2-one (**3m**)

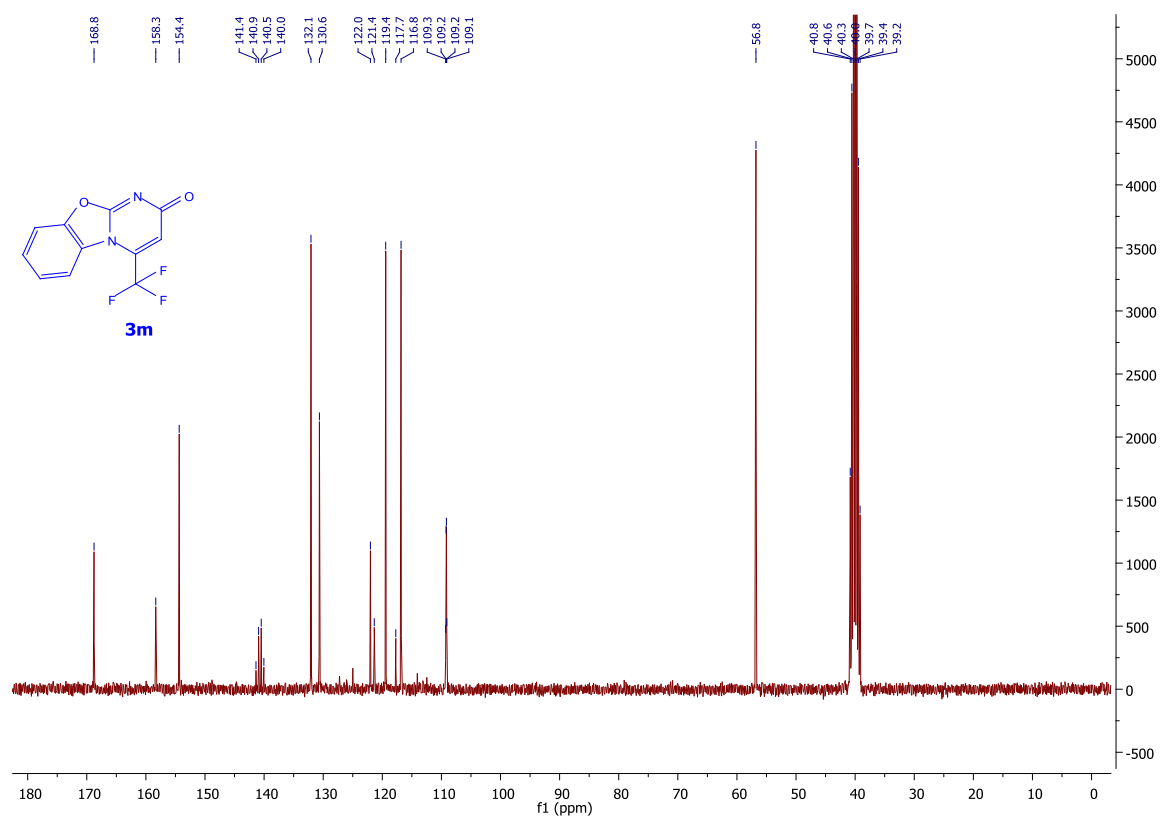
$^1\text{H}$  NMR (300 MHz,  $\text{DMSO}-d_6$ )



<sup>19</sup>F NMR (282 MHz, DMSO-*d*<sub>6</sub>)

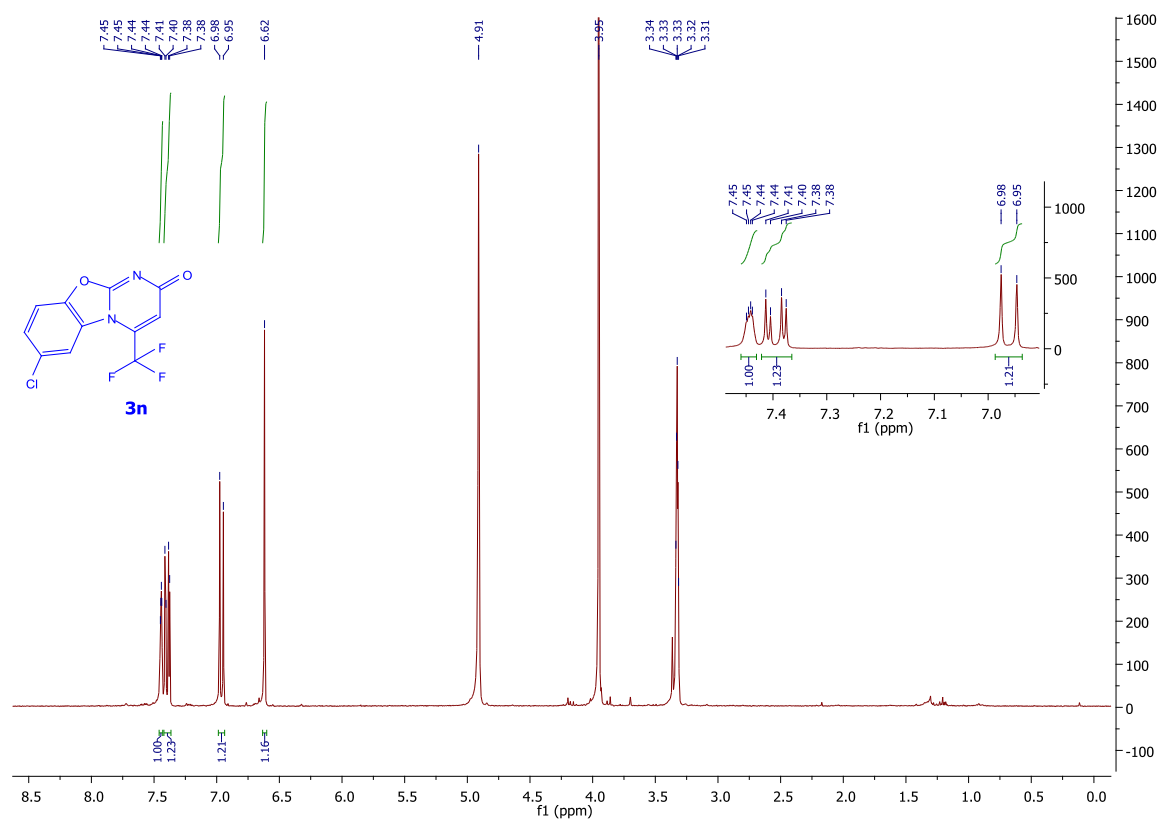


<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)



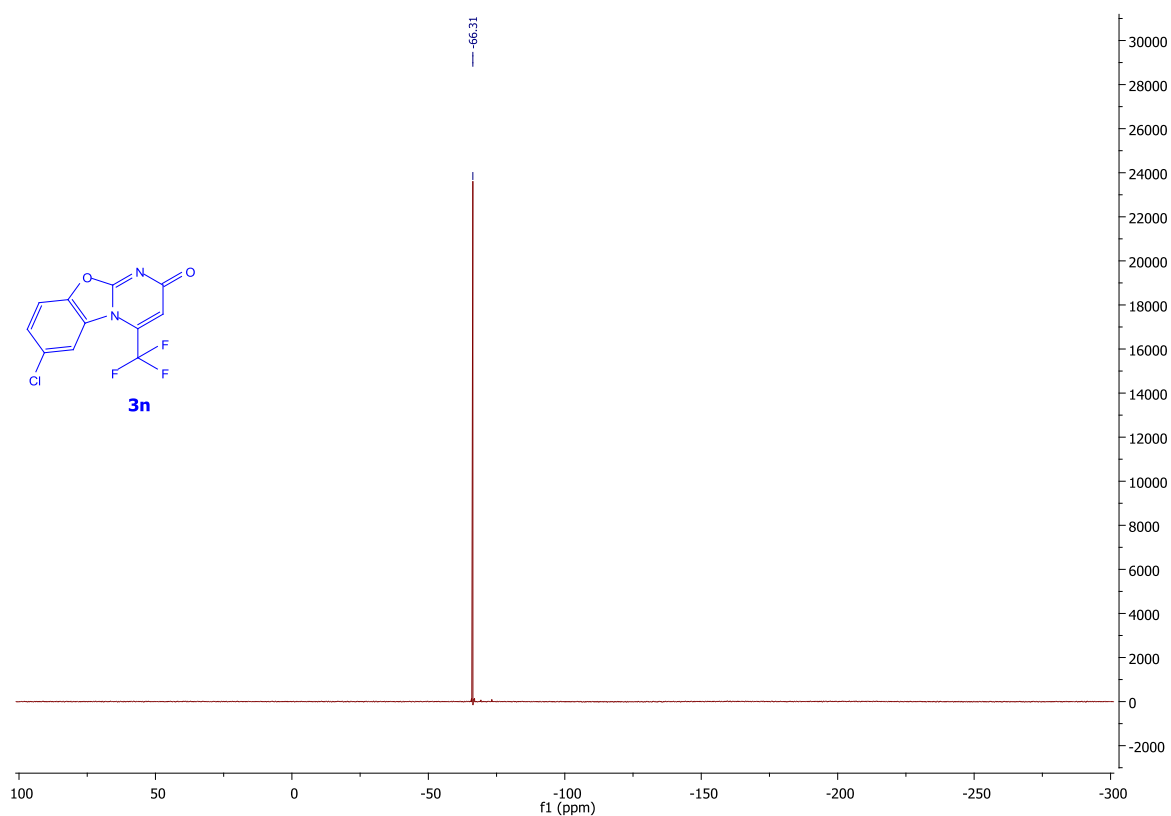
7-chloro-4-(trifluoromethyl)-2H-benzo[4,5]oxazolo[3,2-a]pyrimidin-2-one (**3n**)

<sup>1</sup>H NMR (300 MHz, MeOH-*d*<sub>4</sub>)

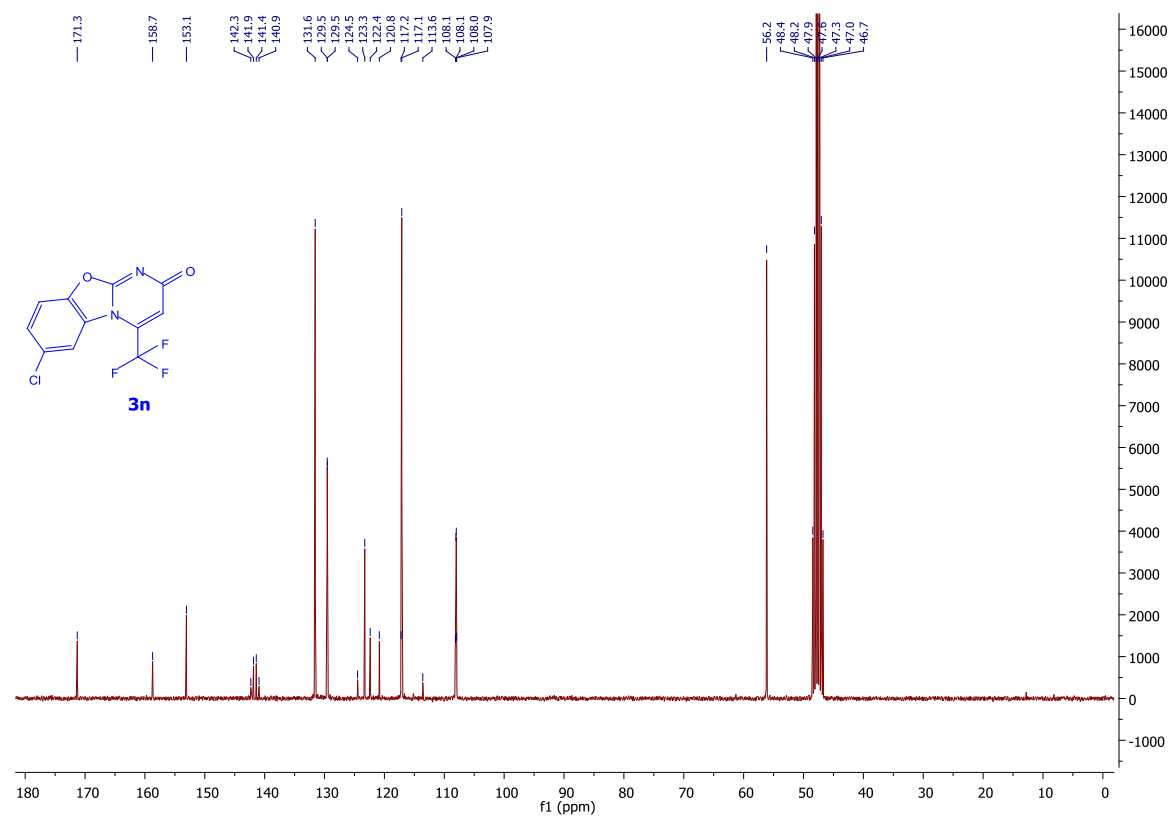




$^{19}\text{F}$  NMR (282 MHz,  $\text{MeOH-}d_4$ )

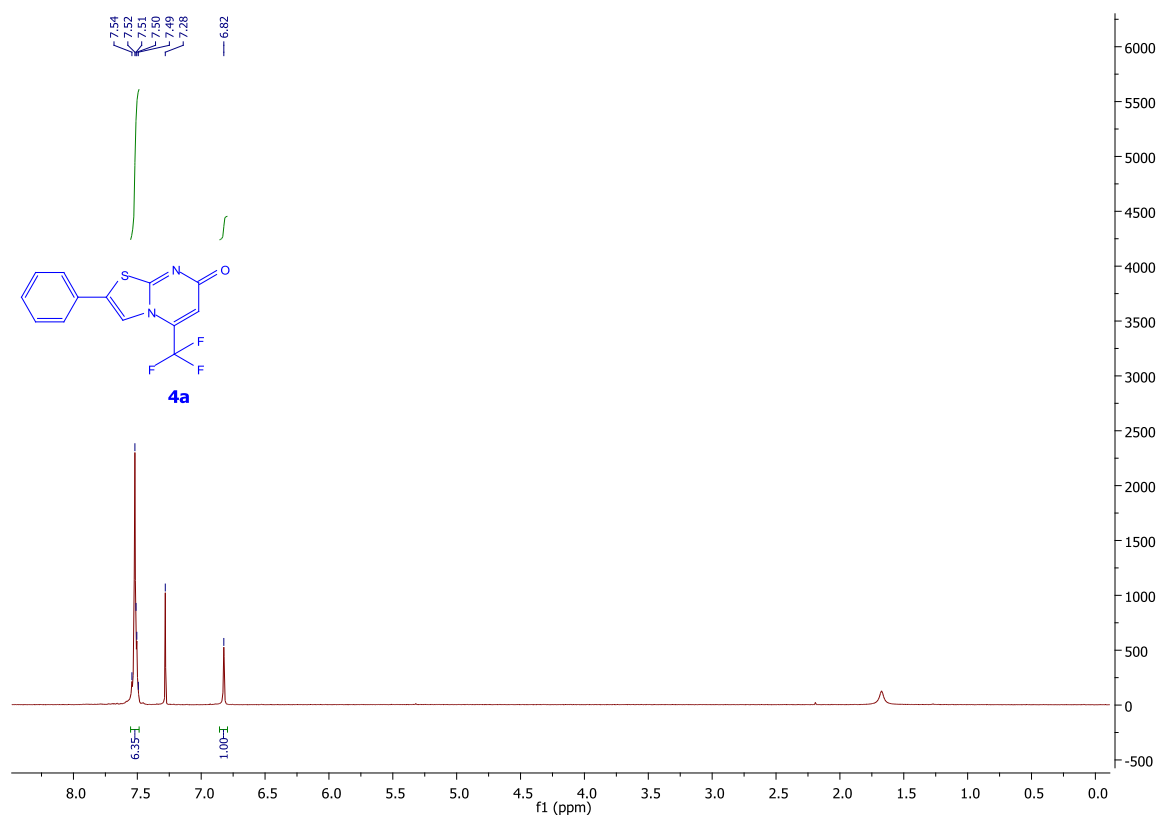


$^{13}\text{C}$  NMR (75 MHz,  $\text{MeOH-}d_4$ )

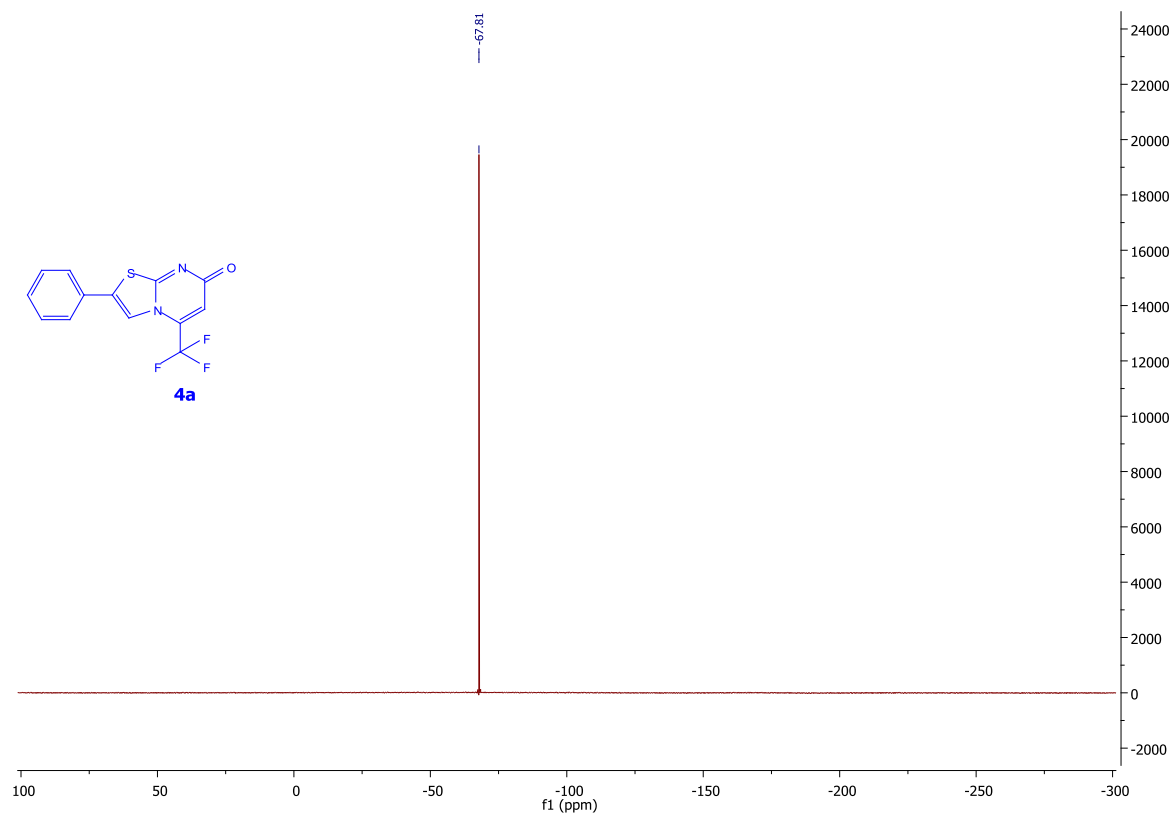


2-phenyl-5-(trifluoromethyl)-7H-thiazolo[3,2-*a*]pyrimidin-7-one (**4a**)

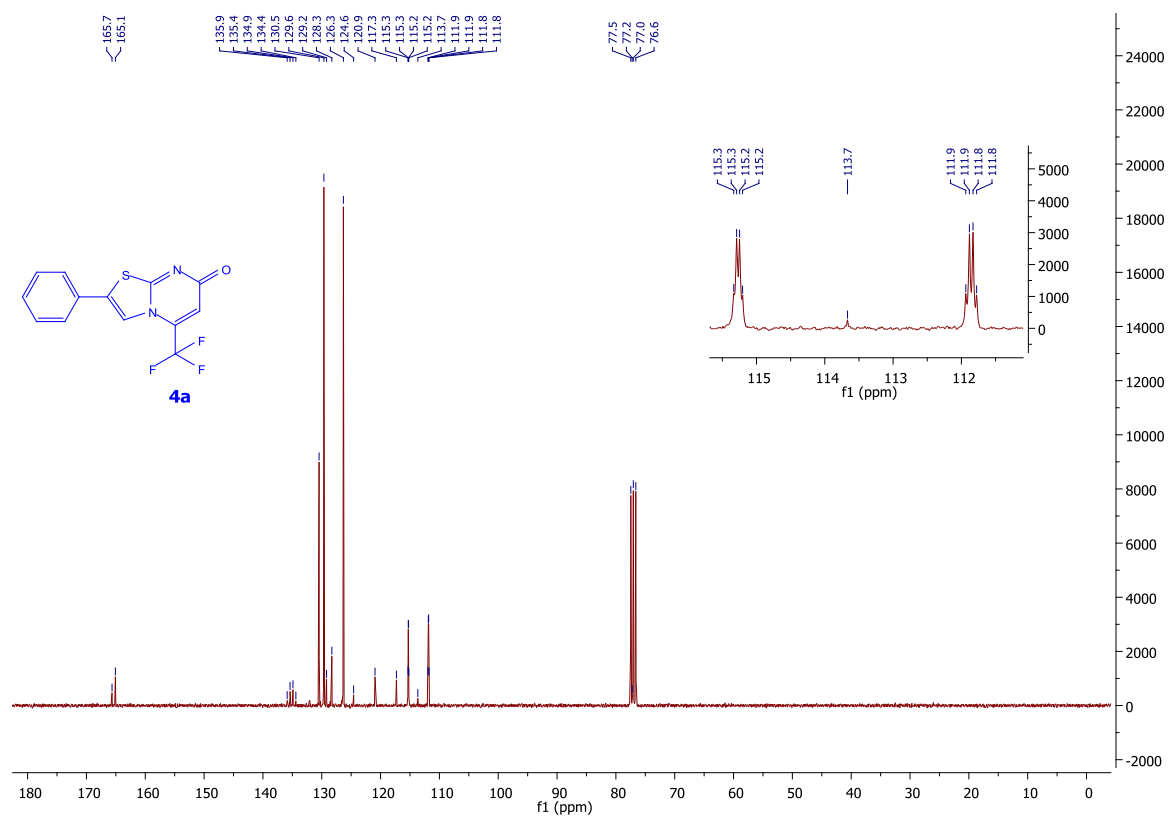
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

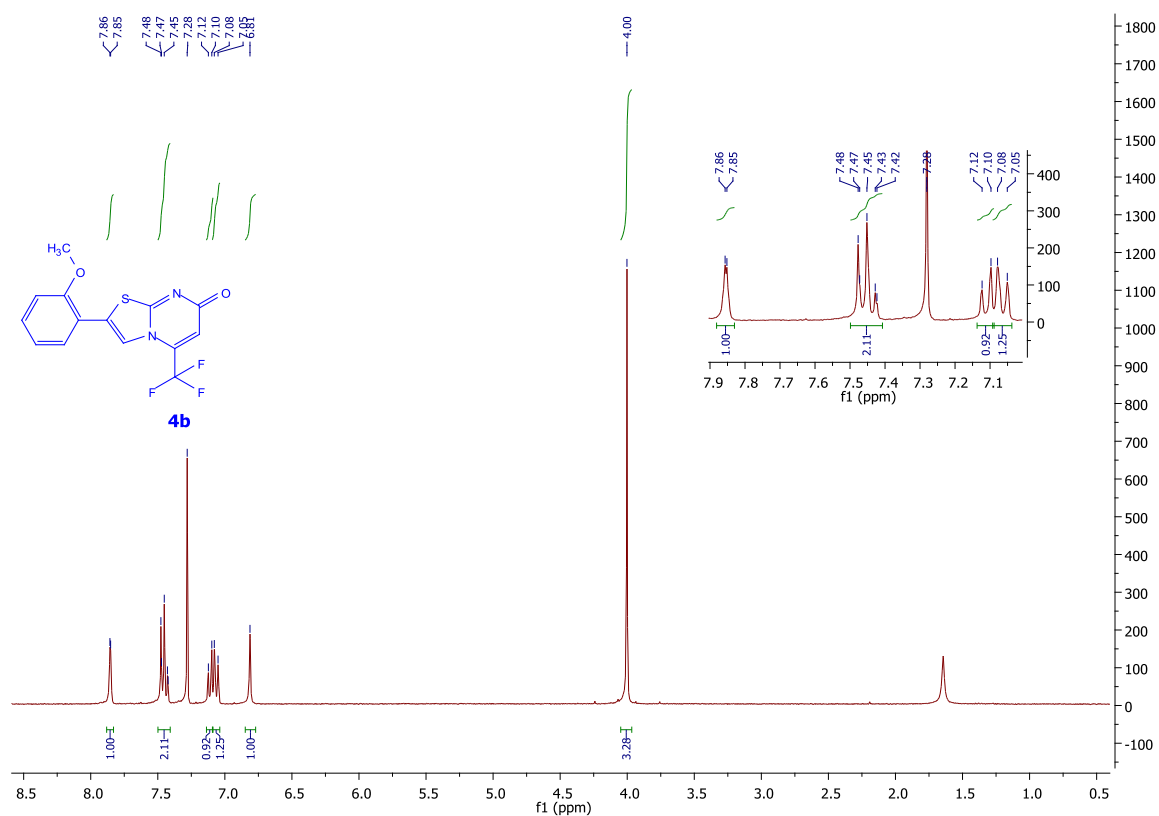


<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

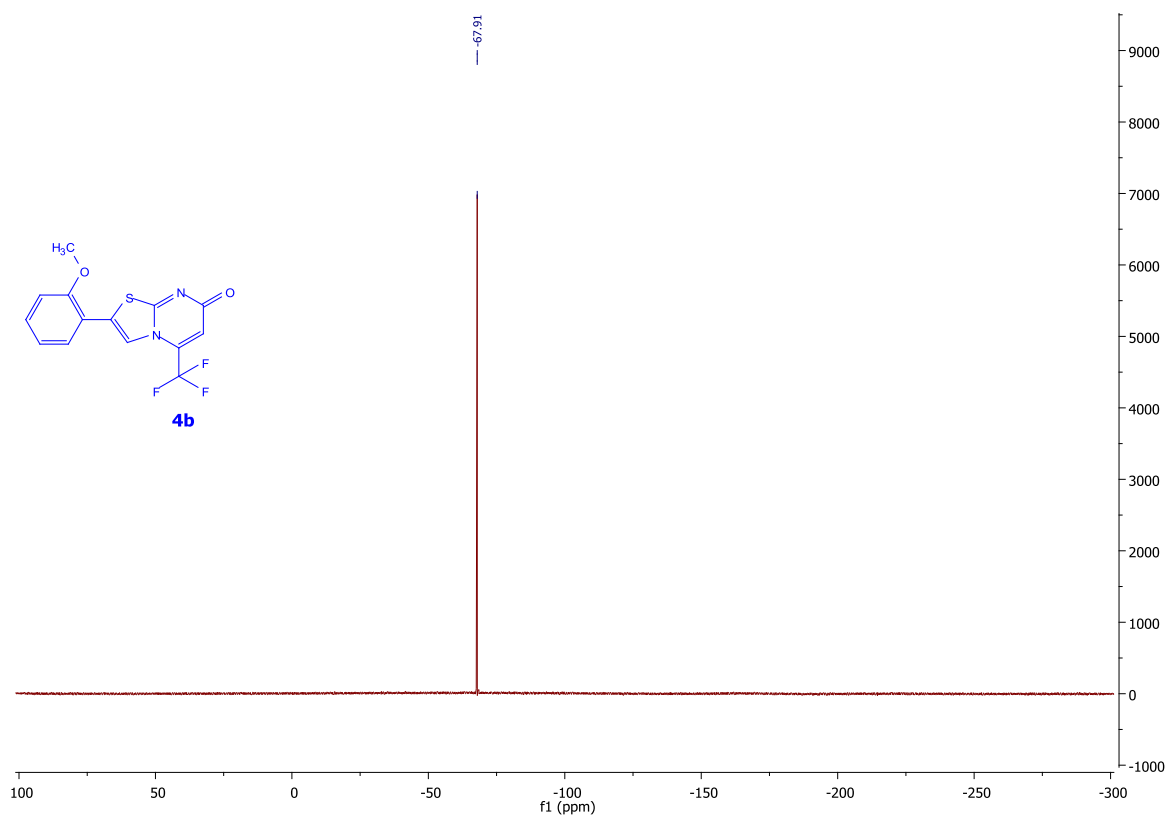


2-(2-methoxyphenyl)-5-(trifluoromethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**4b**)

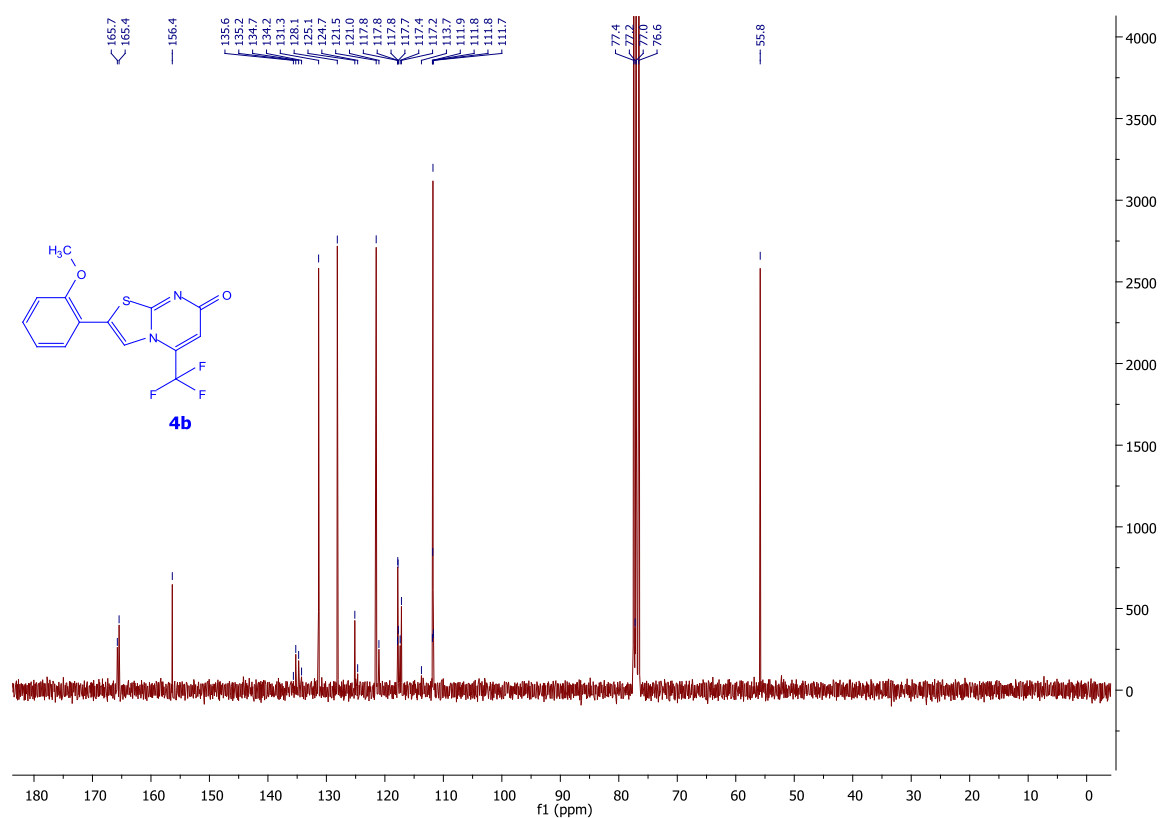
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

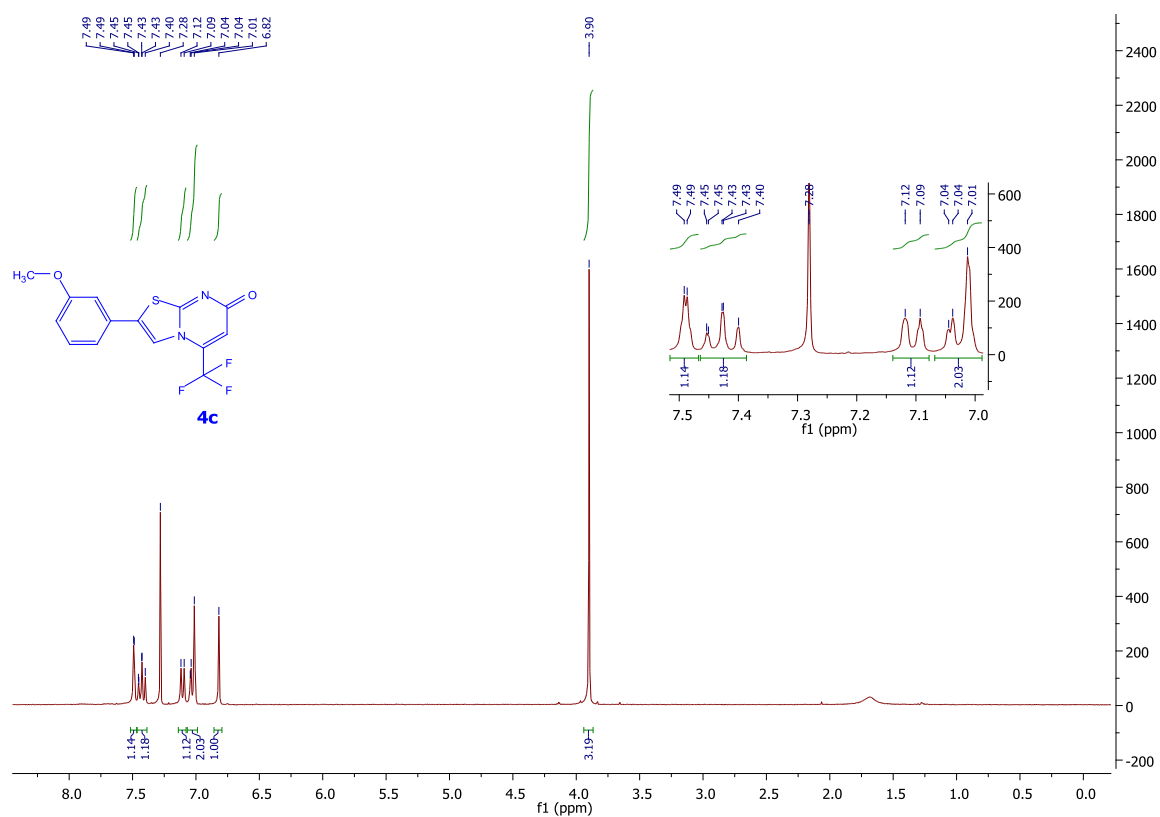


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

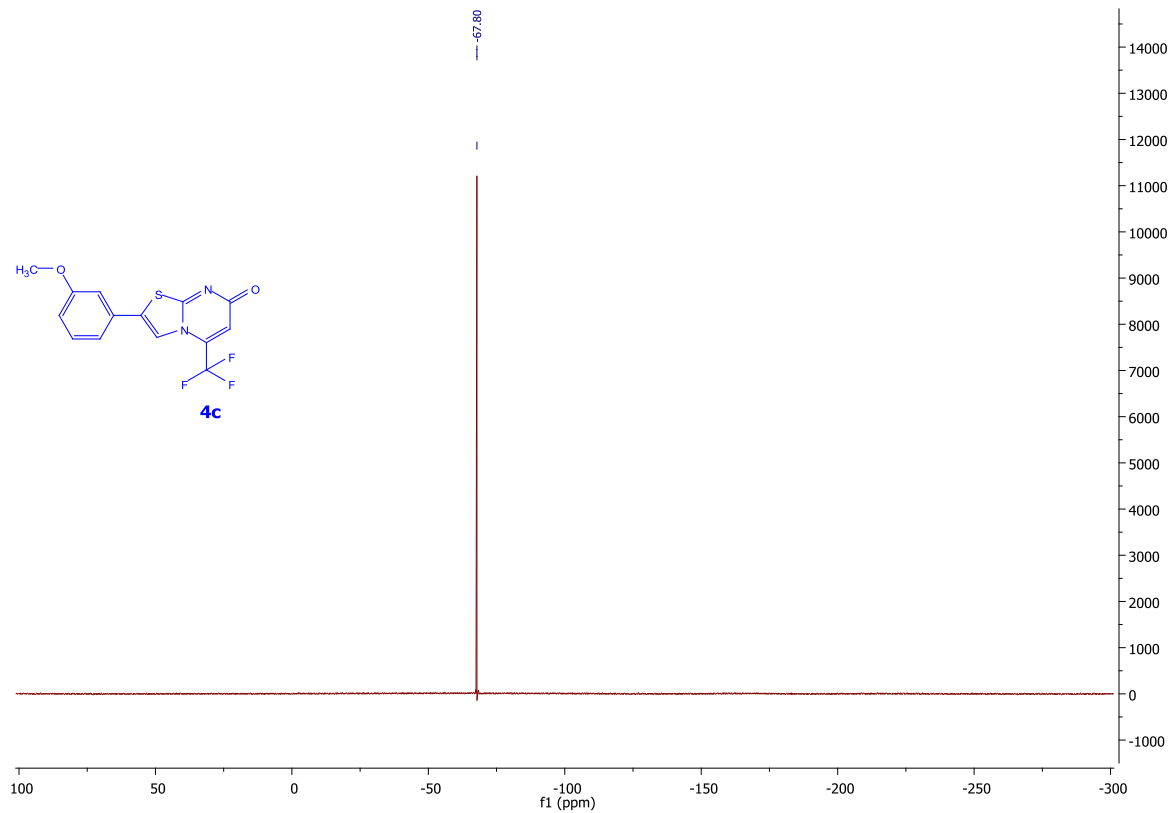


2-(3-methoxyphenyl)-5-(trifluoromethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**4c**)

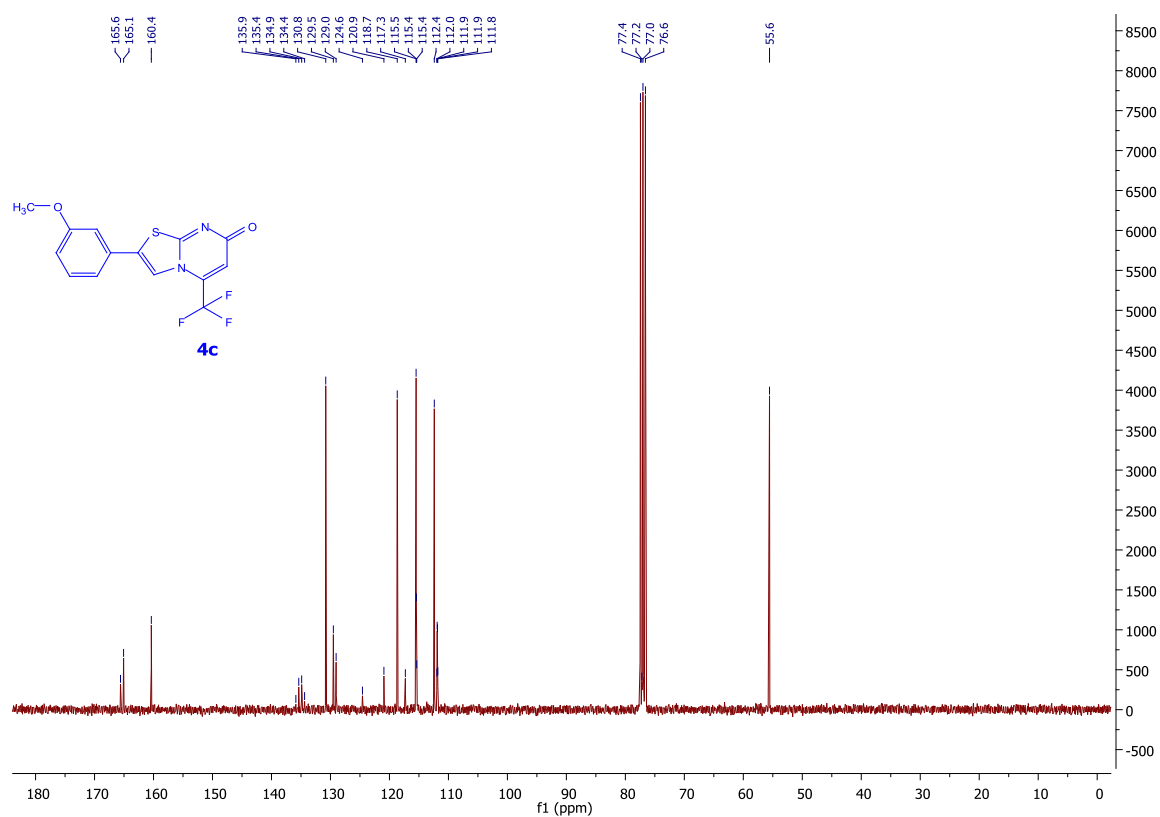
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



<sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>)

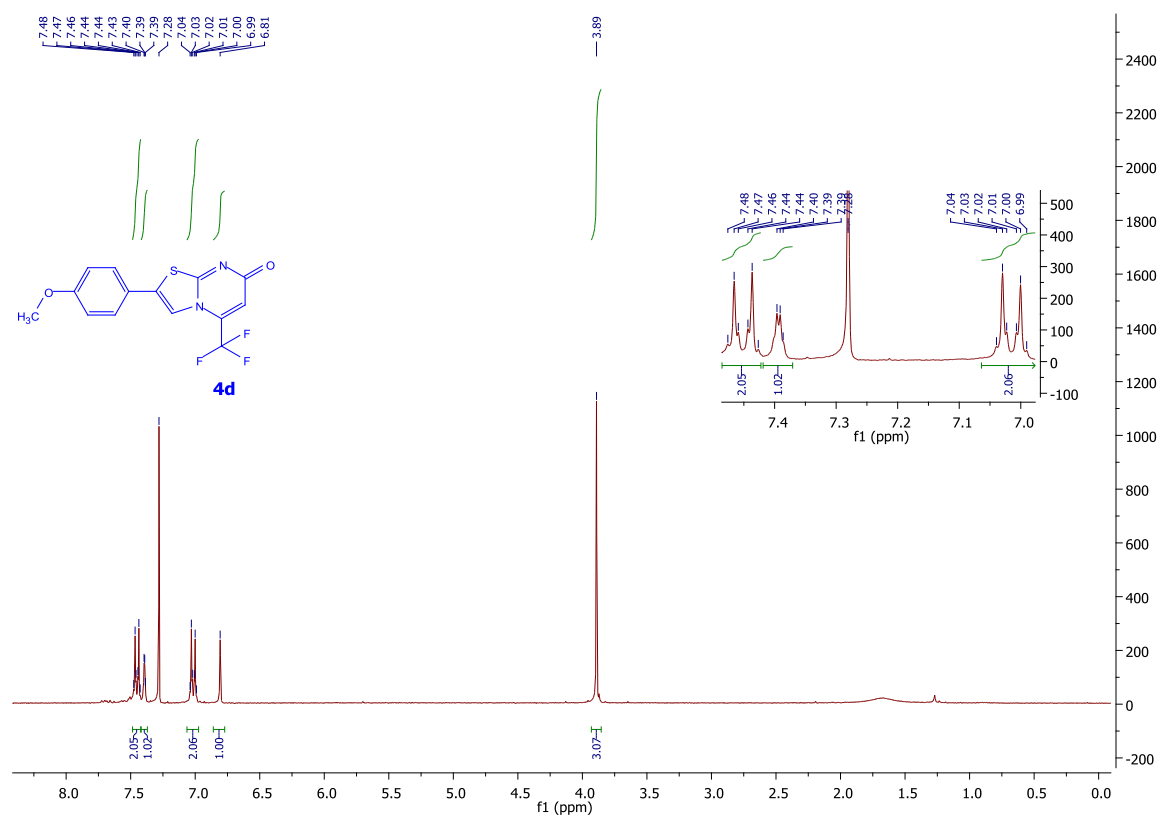


<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

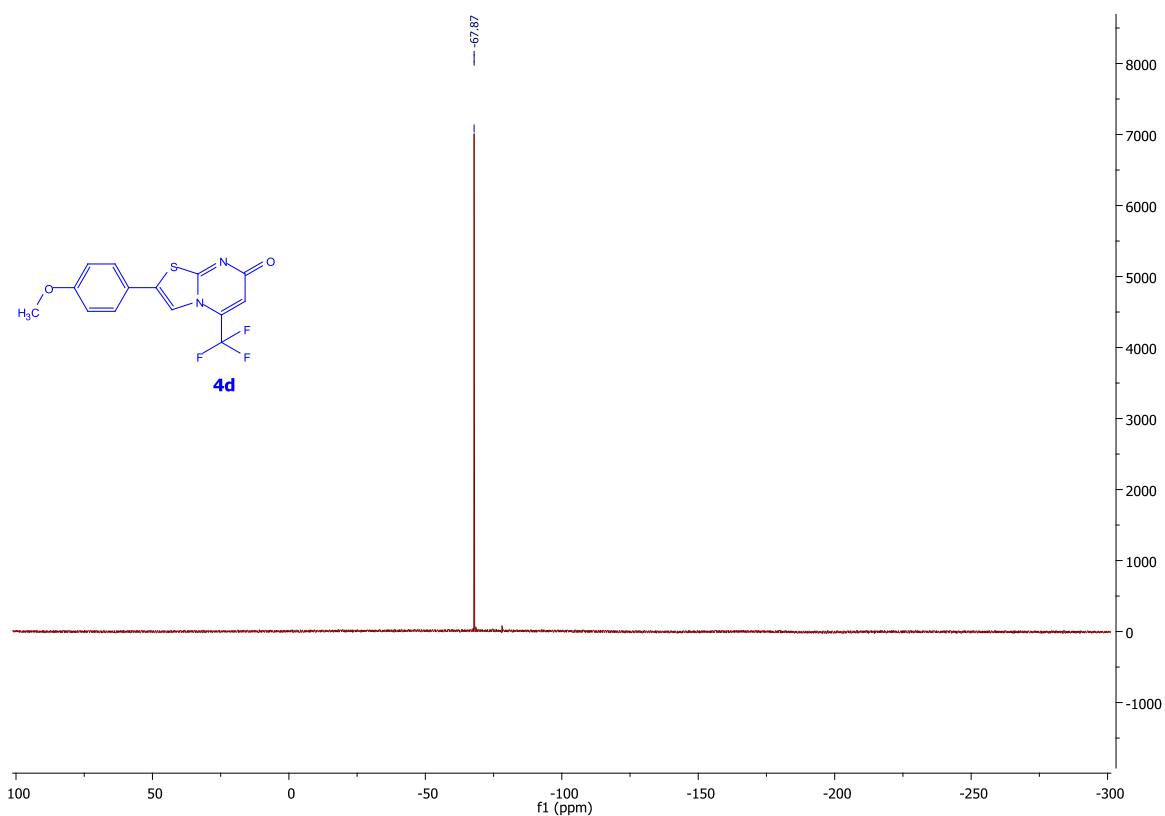


## 2-(4-methoxyphenyl)-5-(trifluoromethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**4d**)

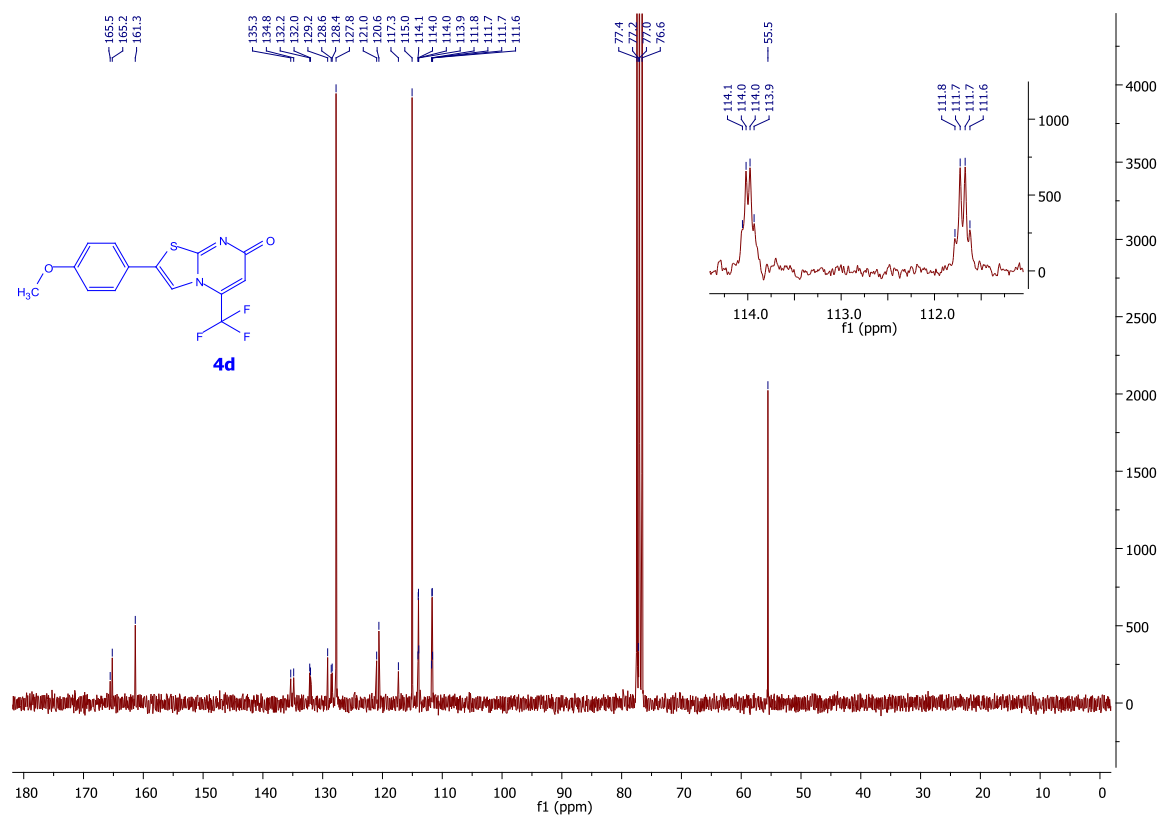
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



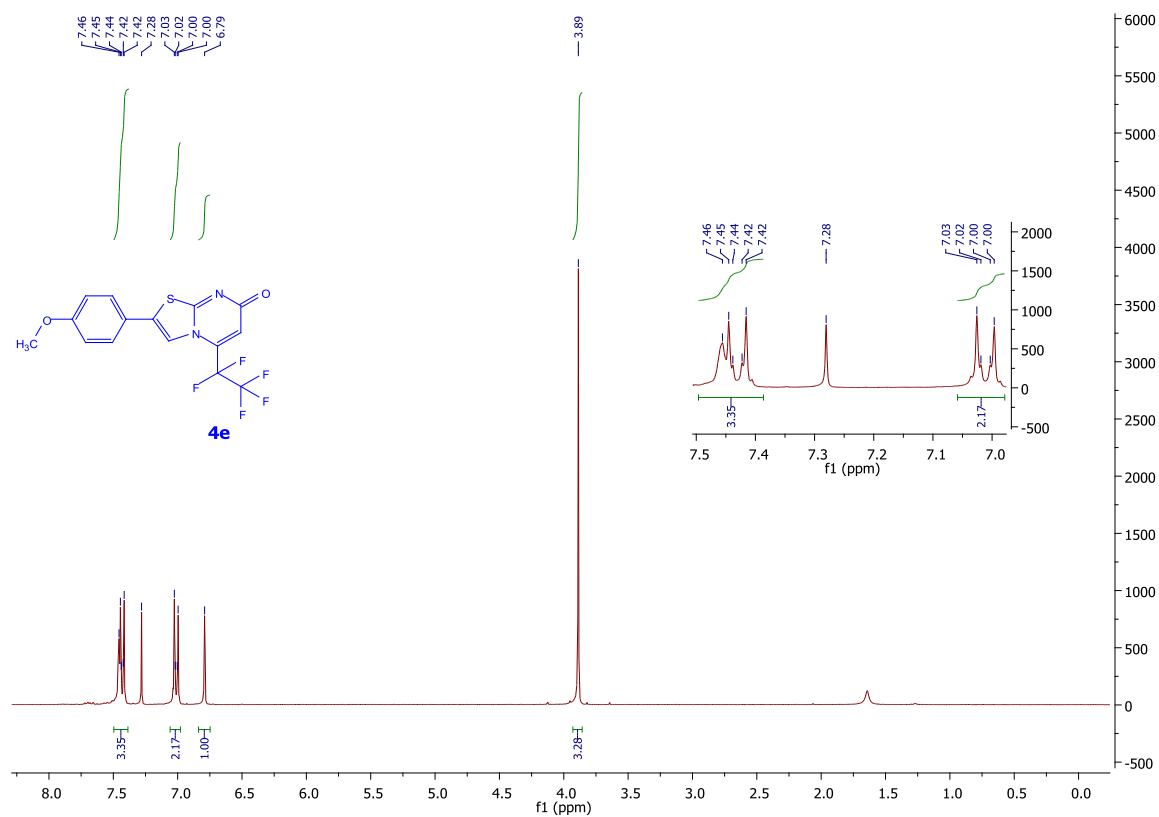
$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



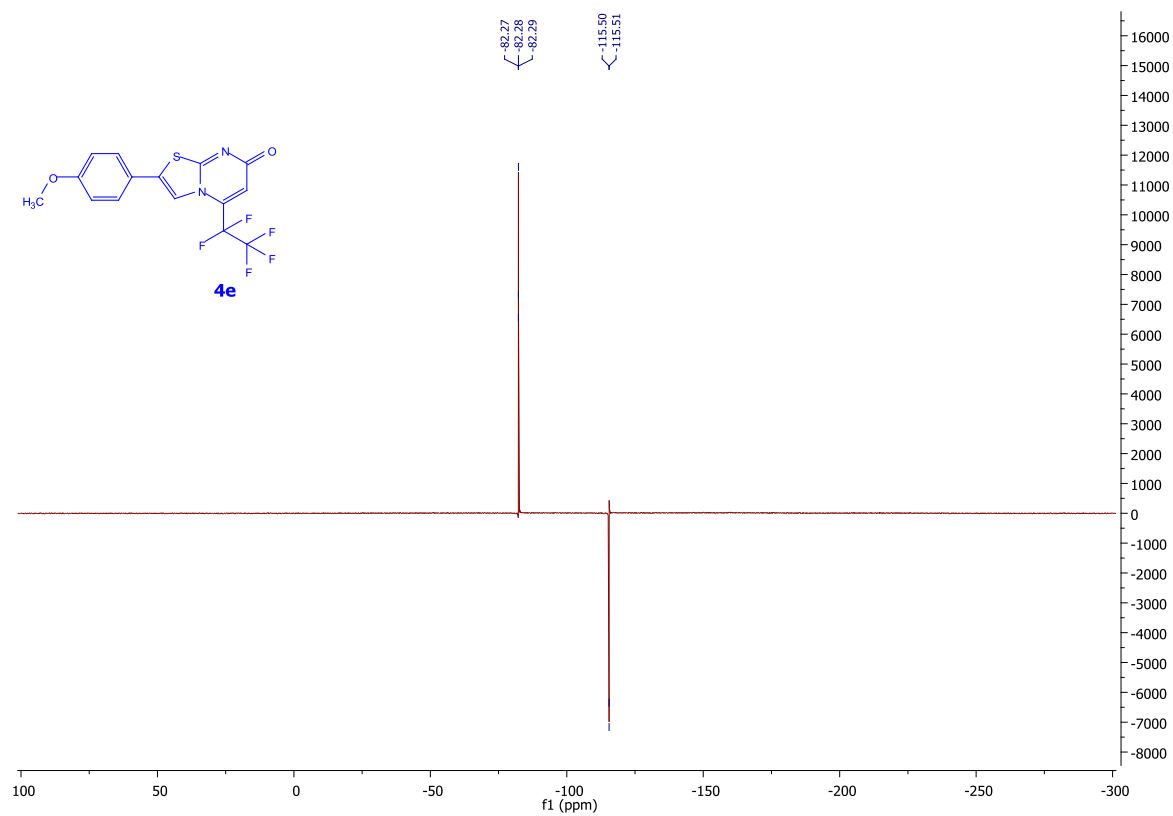


2-(4-methoxyphenyl)-5-(perfluoroethyl)-7H-thiazolo[3,2-*a*]pyrimidin-7-one (**4e**)

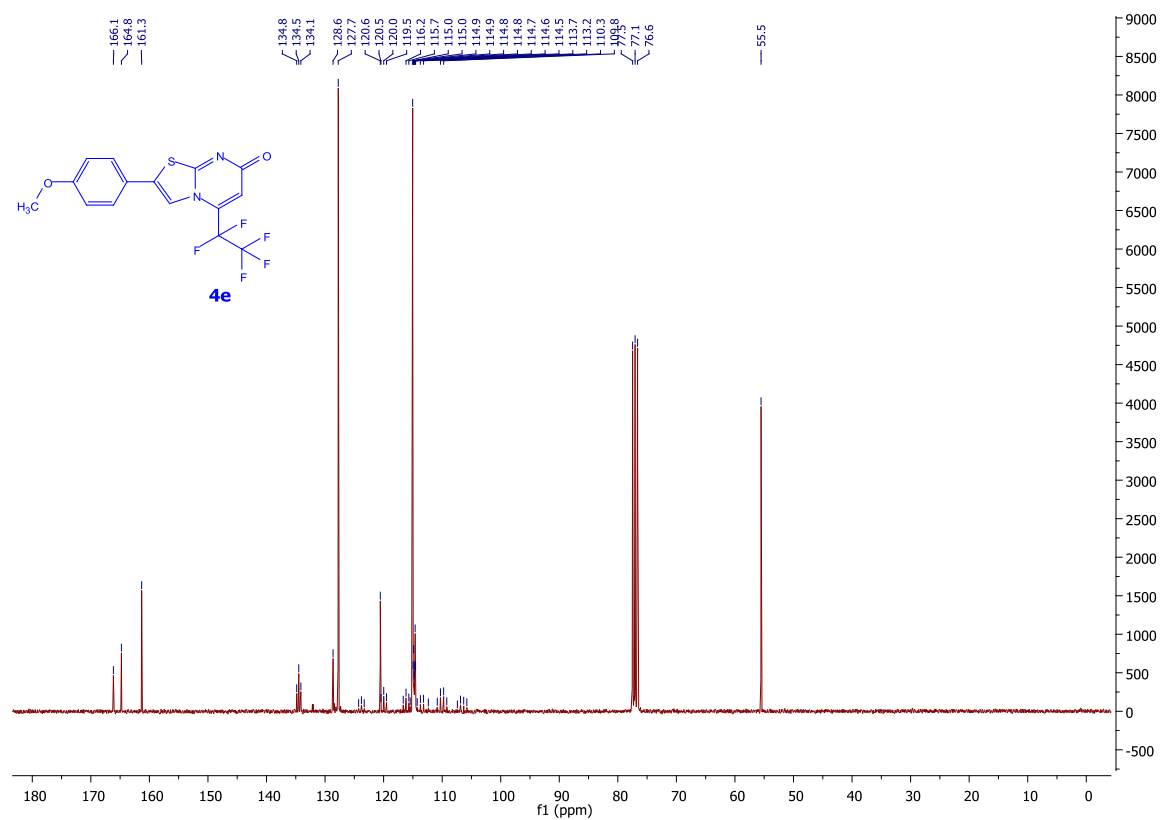
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

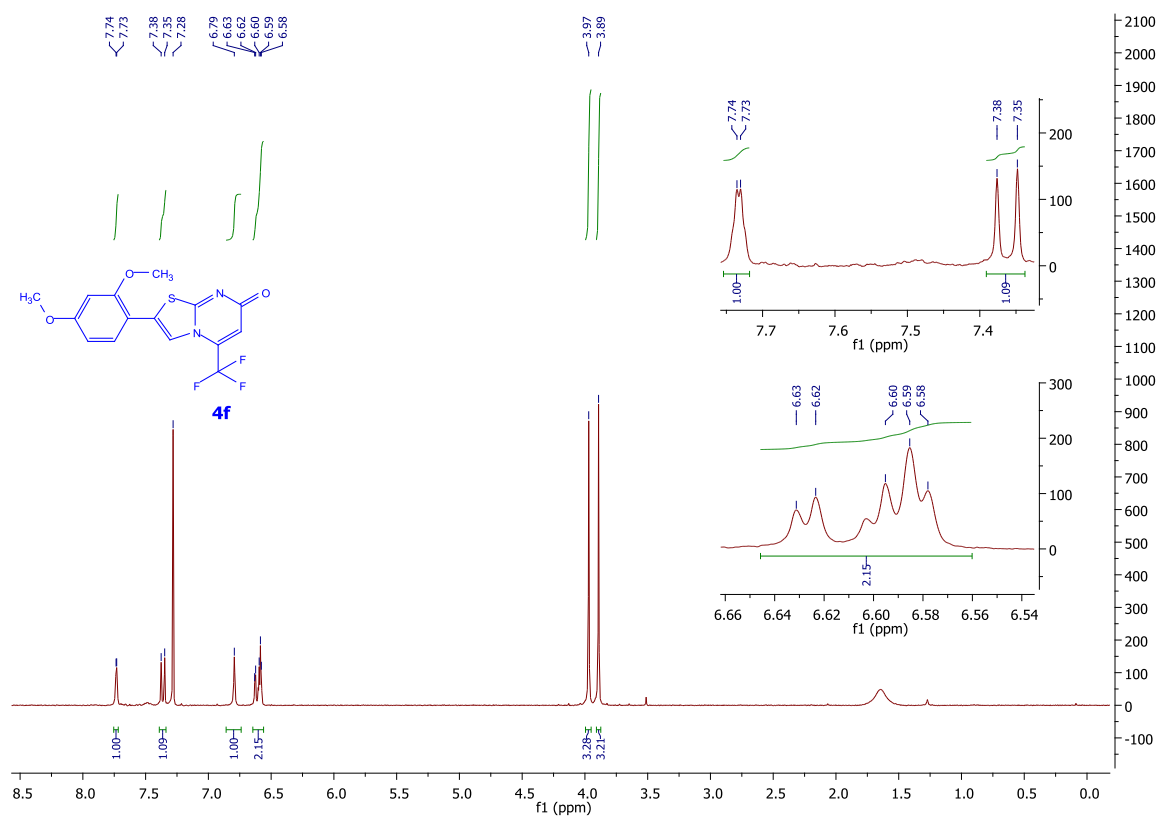


<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

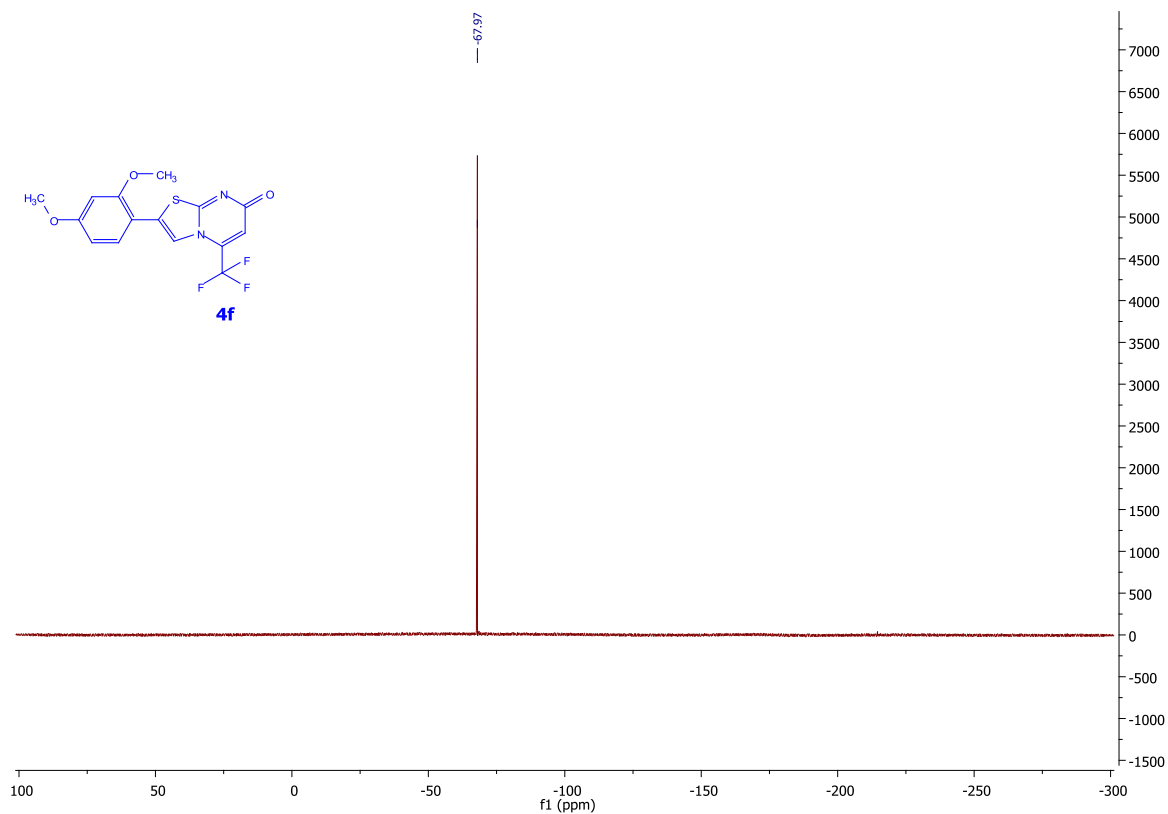


2-(2,4-dimethoxyphenyl)-5-(trifluoromethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**4f**)

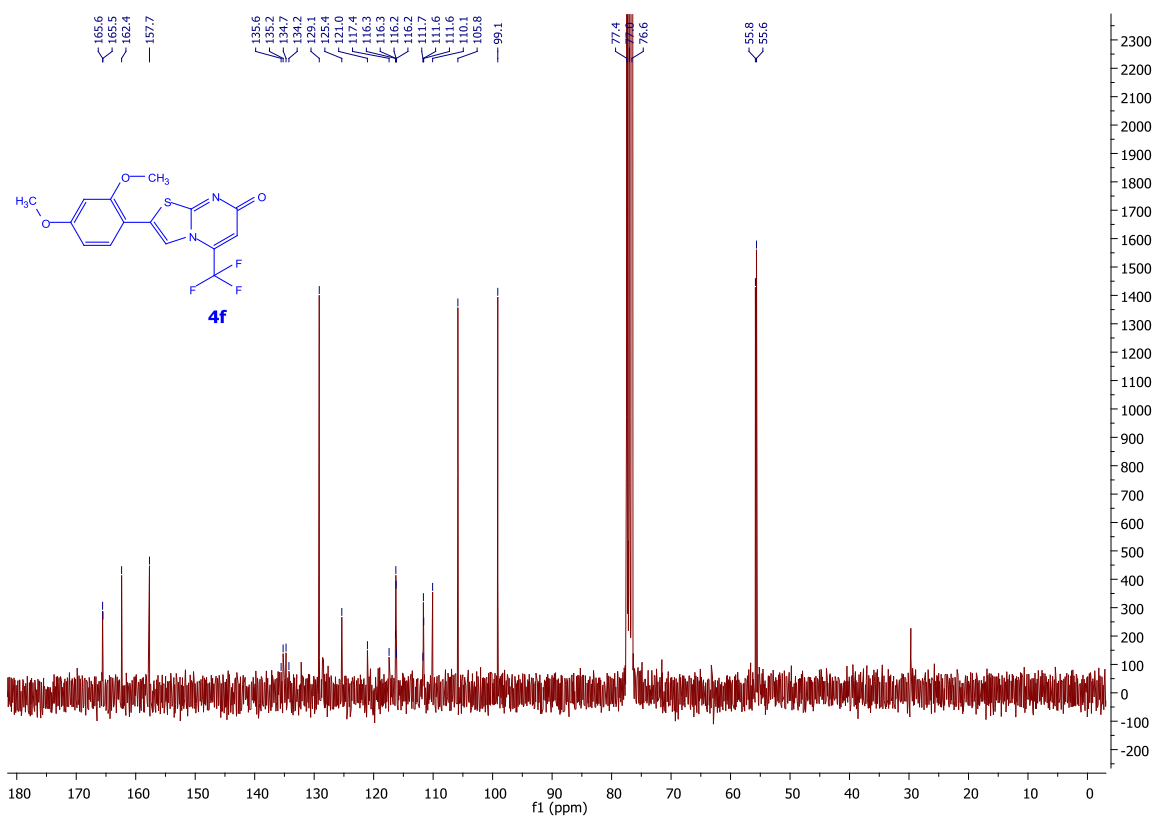
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

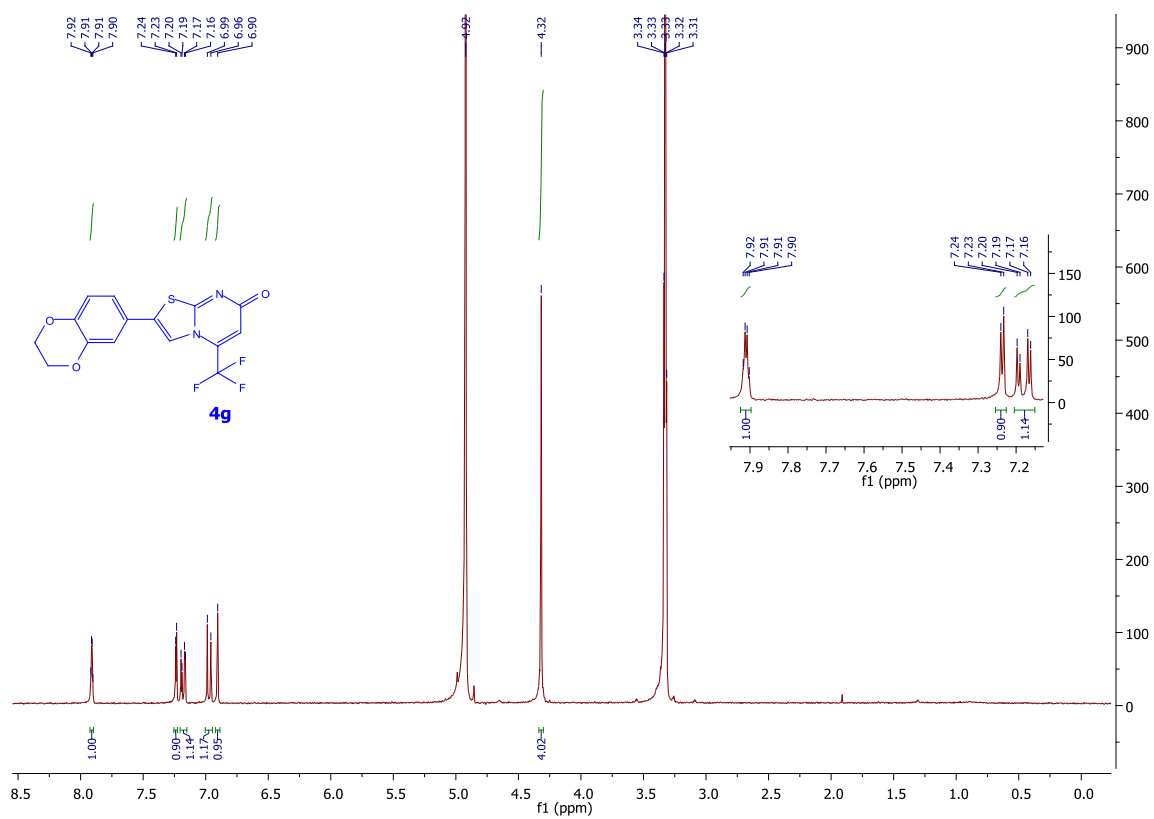


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

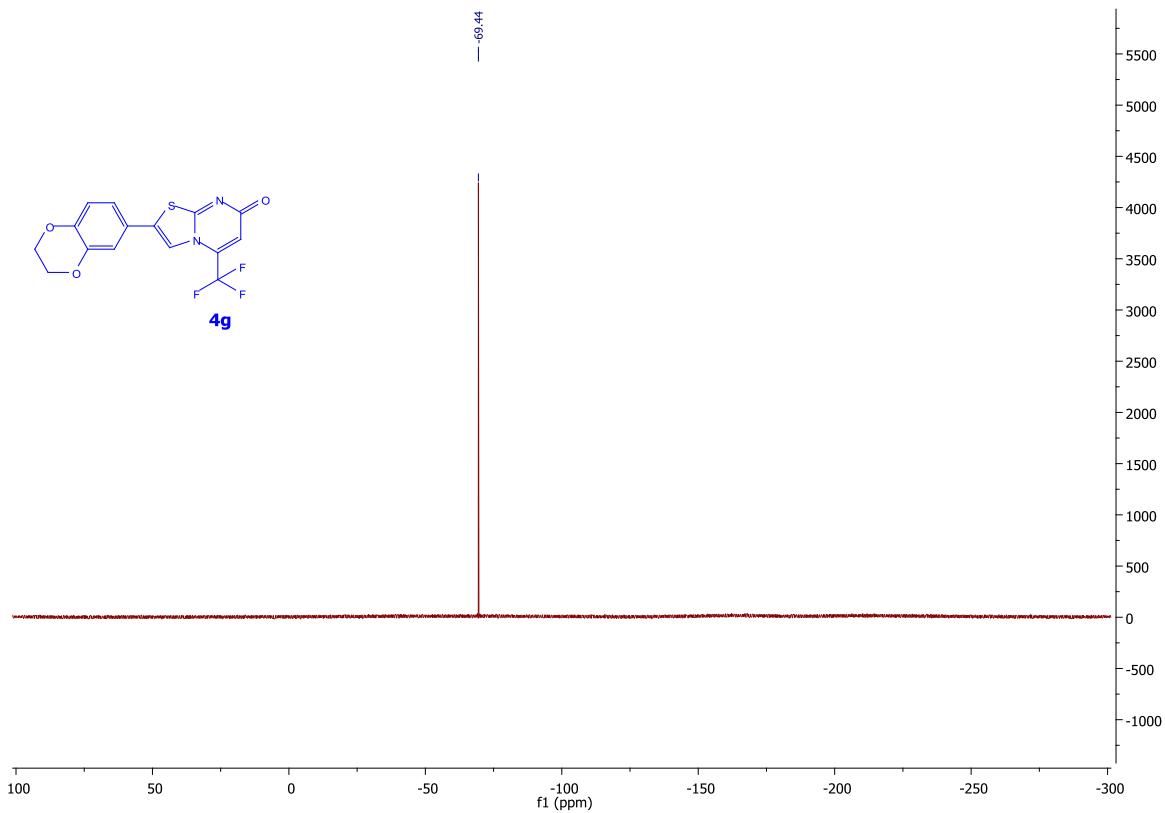


2-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-5-(trifluoromethyl)-7H-thiazolo[3,2-*a*]pyrimidin-7-one (**4g**)

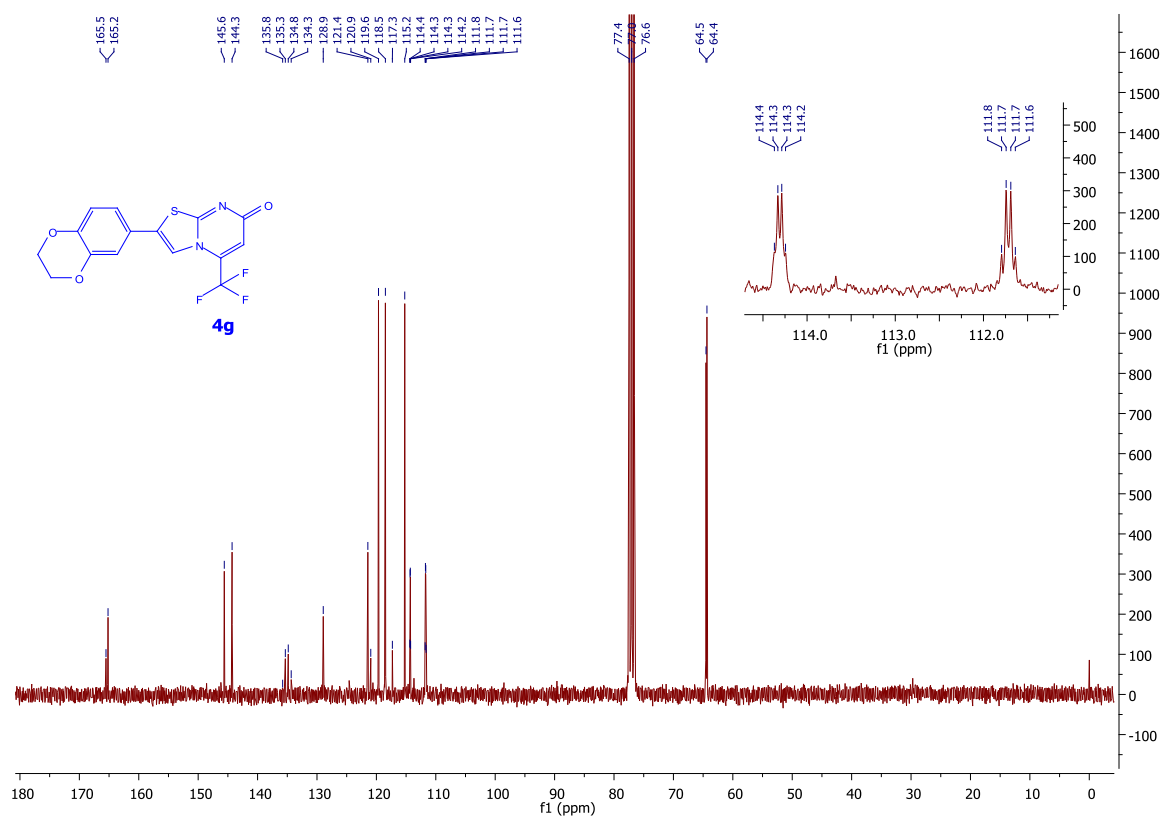
$^1\text{H}$  NMR (300 MHz,  $\text{MeOH-}d_4$ )



**<sup>19</sup>F NMR (282 MHz, MeOH-*d*<sub>4</sub>)**

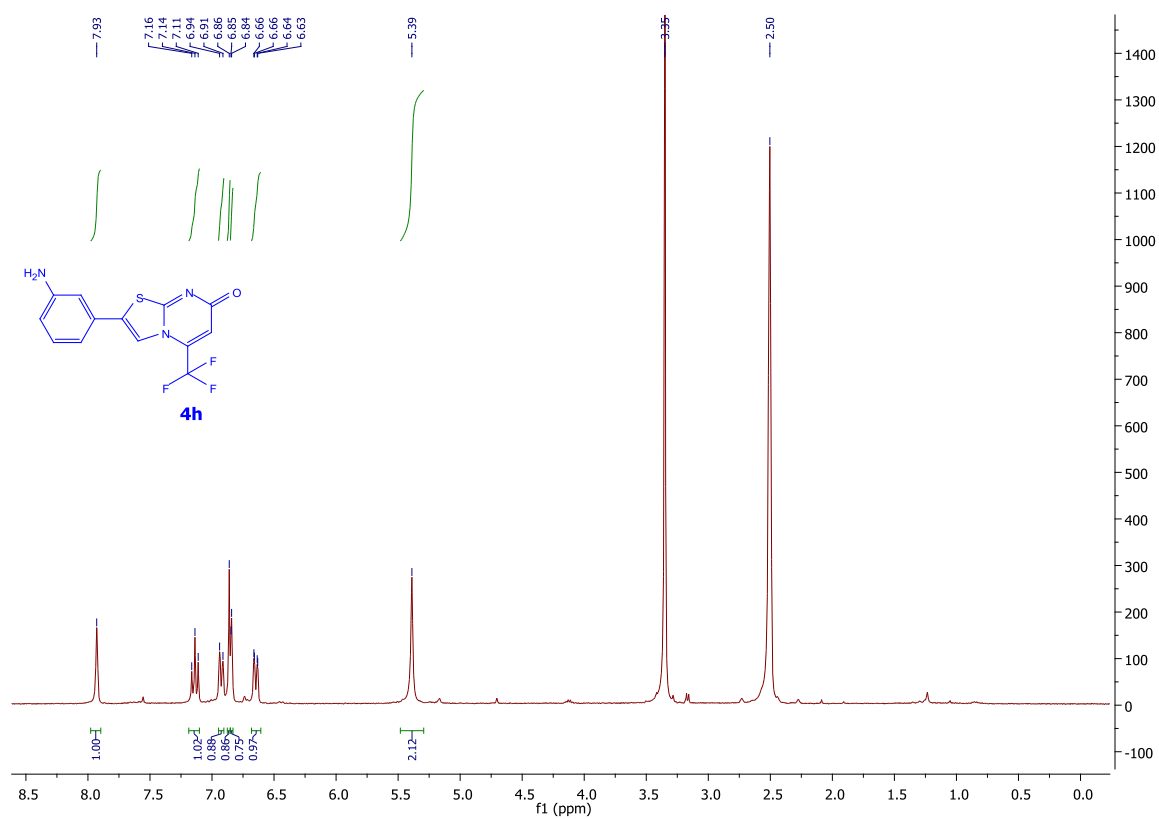


**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)**

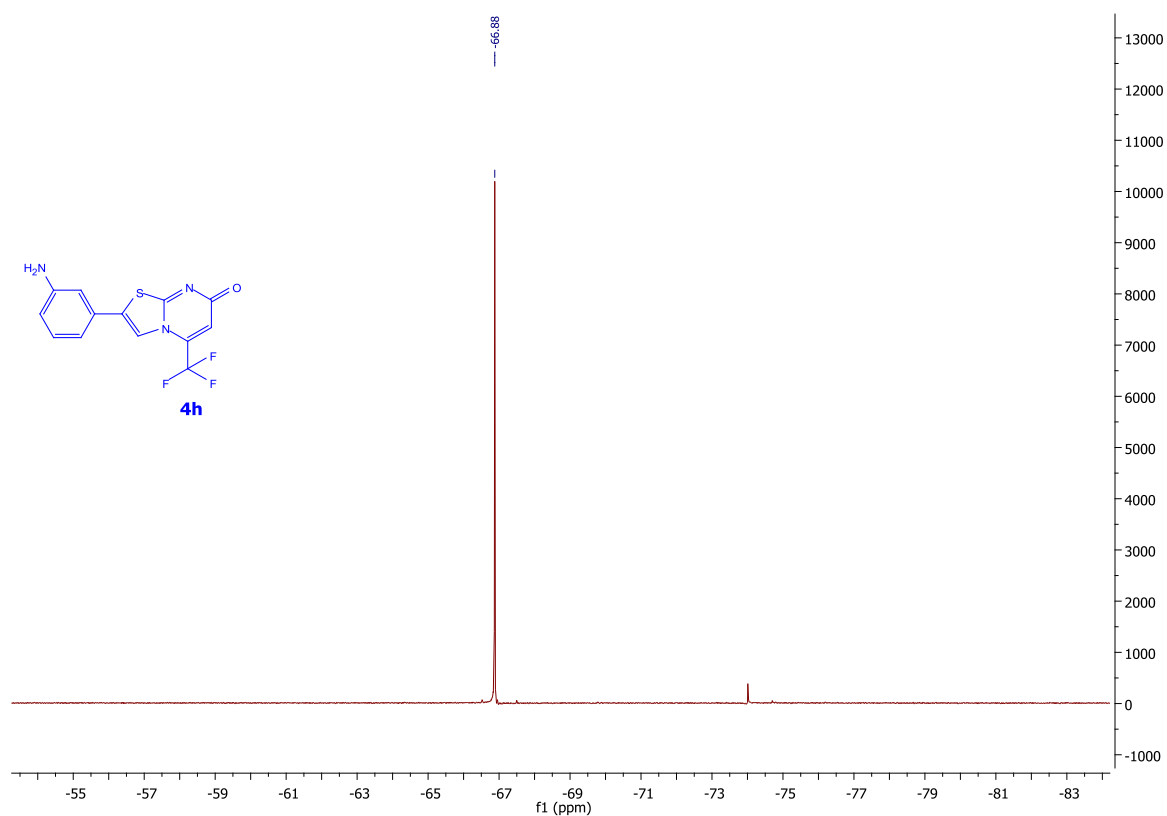


# 2-(3-aminophenyl)-5-(trifluoromethyl)-7*H*-thiazolo[3,2-*a*]pyrimidin-7-one (**4h**)

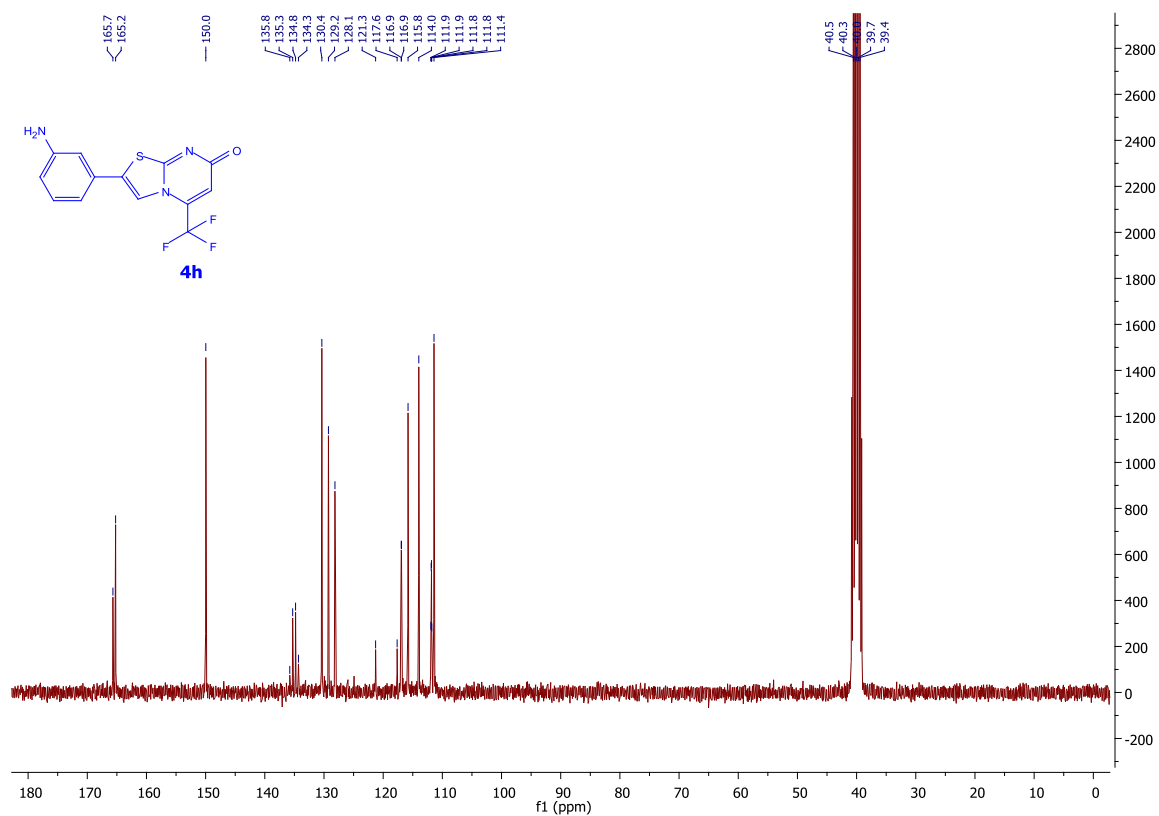
<sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)



$^{19}\text{F}$  NMR (282 MHz,  $\text{DMSO}-d_6$ )

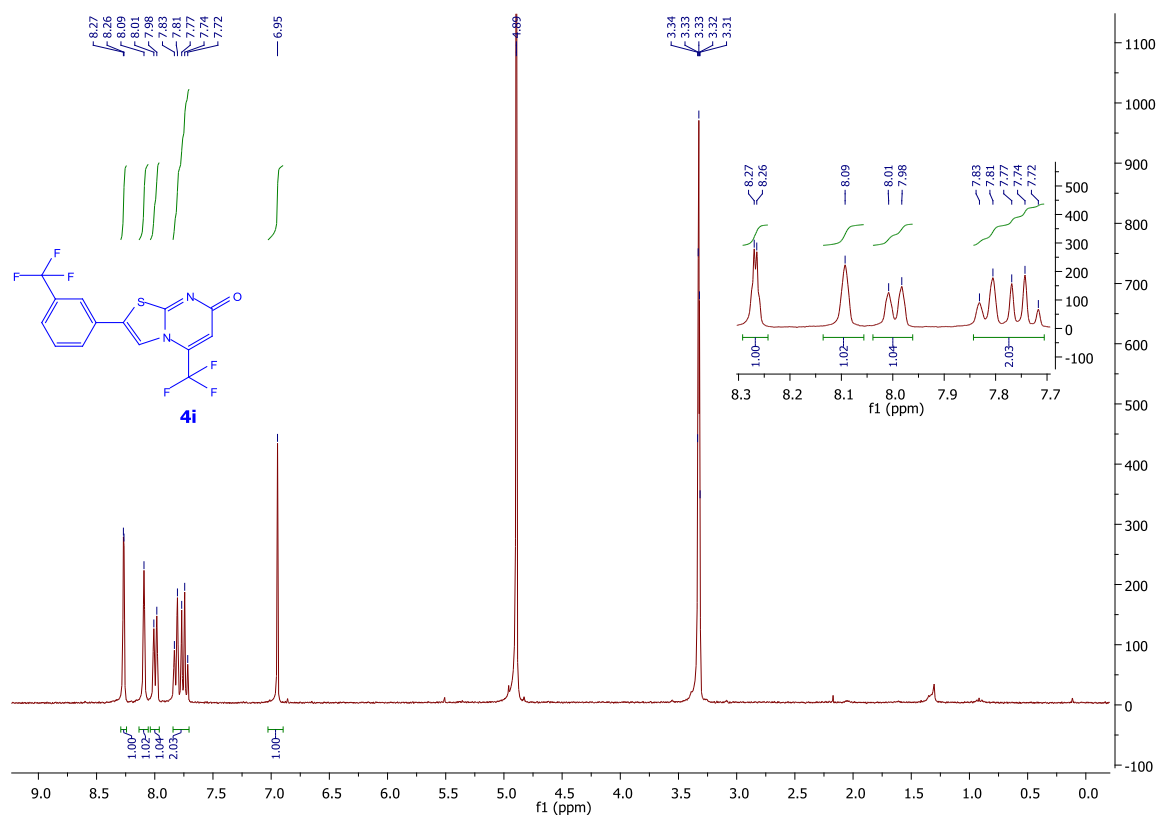


$^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ )



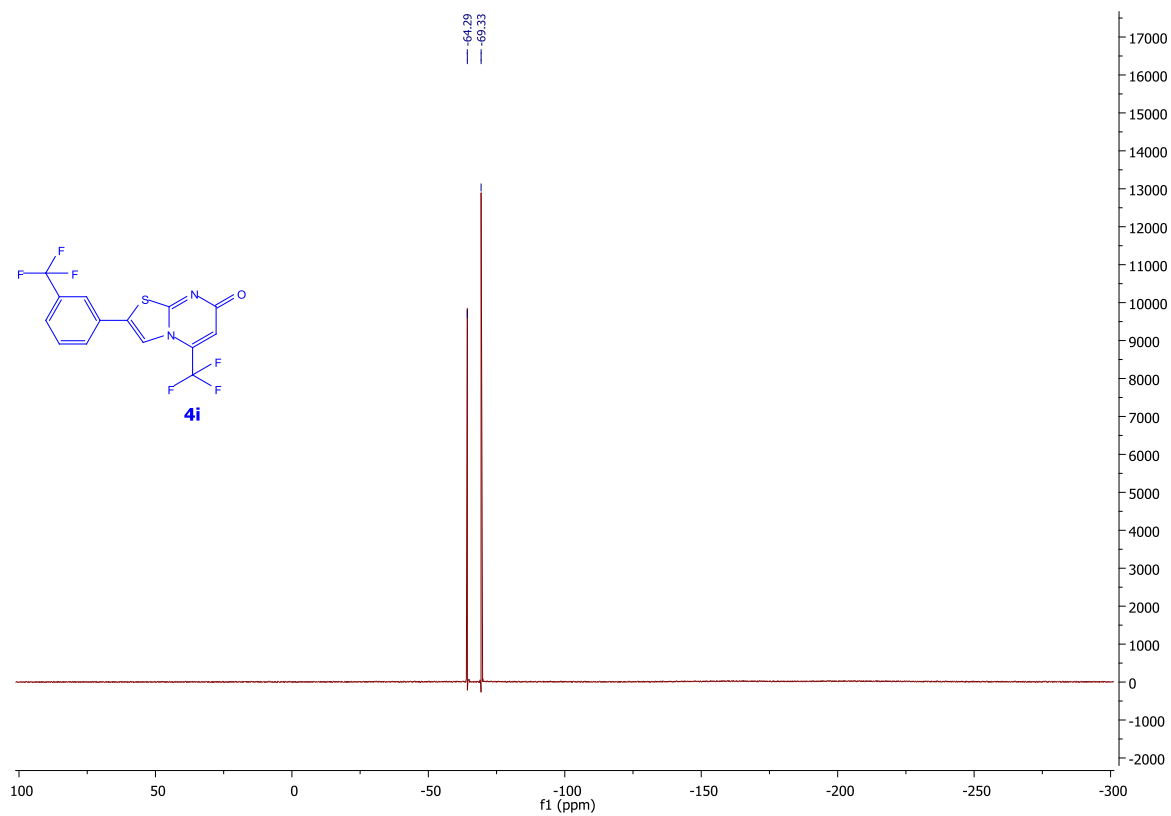
5-(trifluoromethyl)-2-(3-(trifluoromethyl)phenyl)-7H-thiazolo[3,2-*a*]pyrimidin-7-one (**4i**)

$^1\text{H}$  NMR (300 MHz,  $\text{MeOH-}d_4$ )

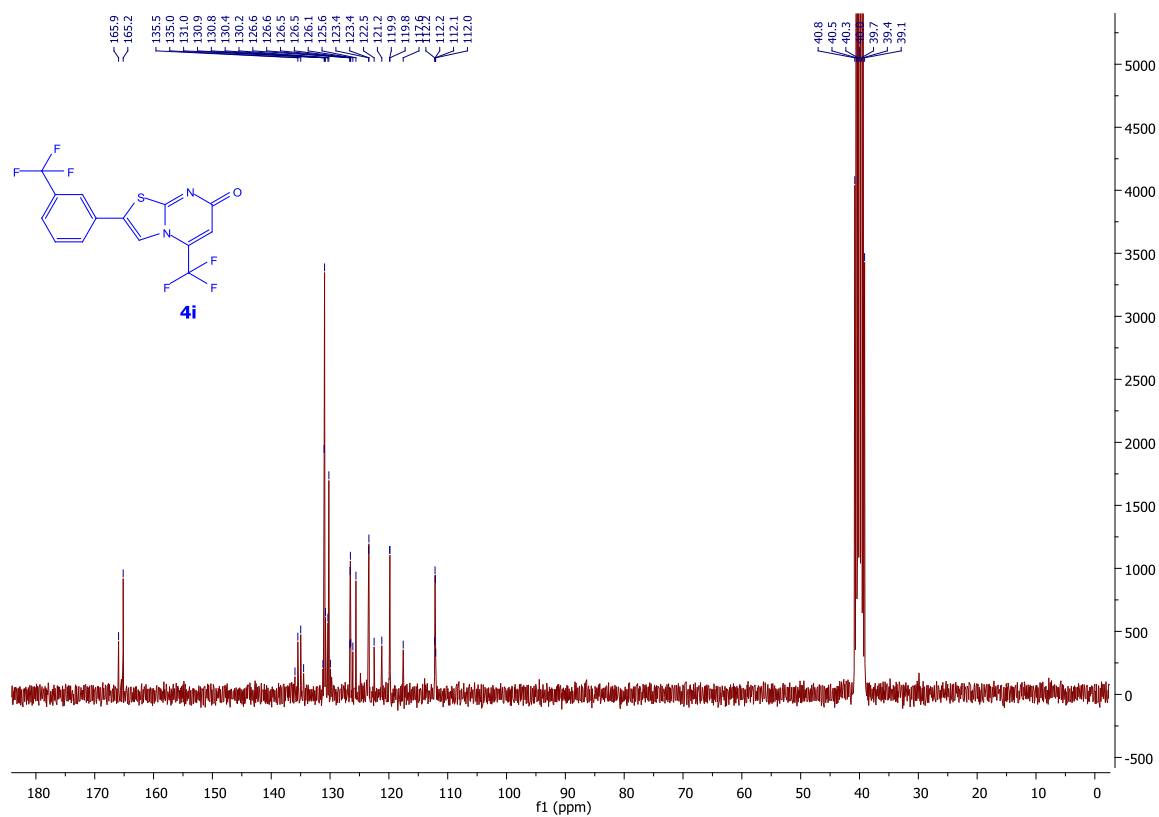


$^{19}\text{F}$  NMR (282 MHz,  $\text{MeOH-}d_4$ )



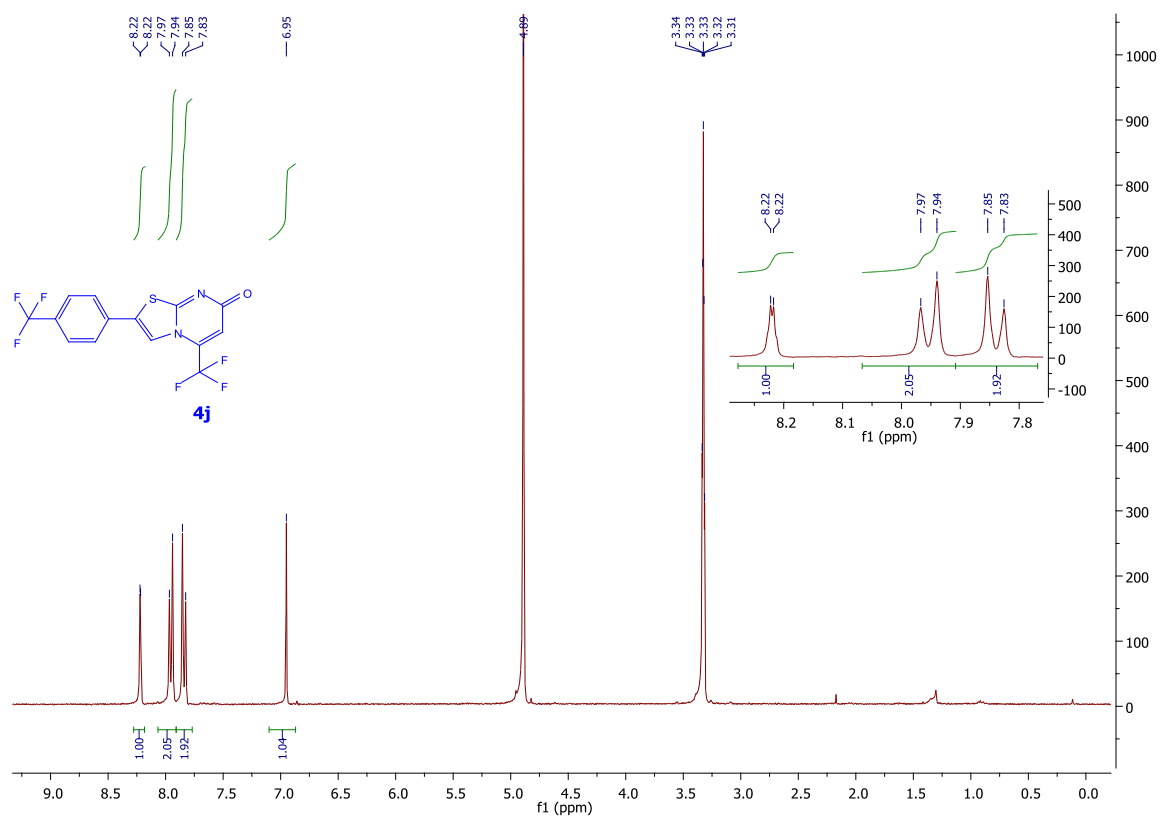


<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)

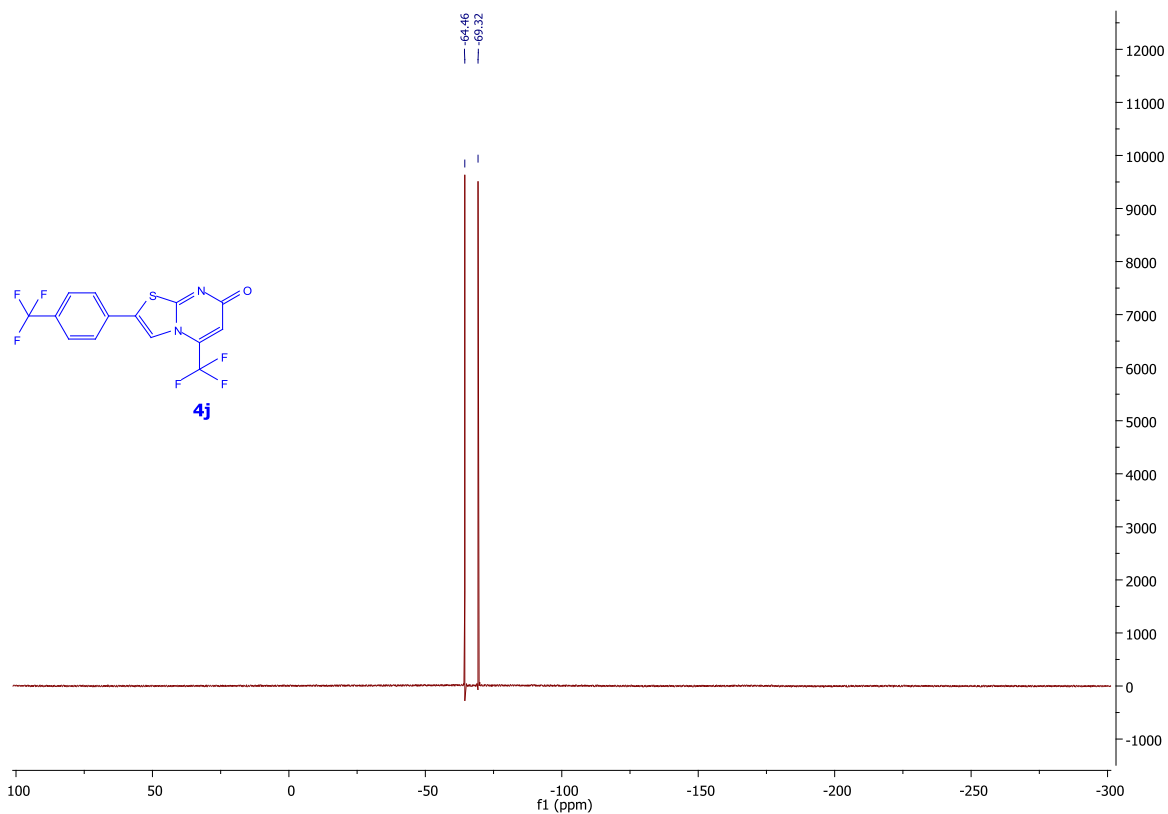


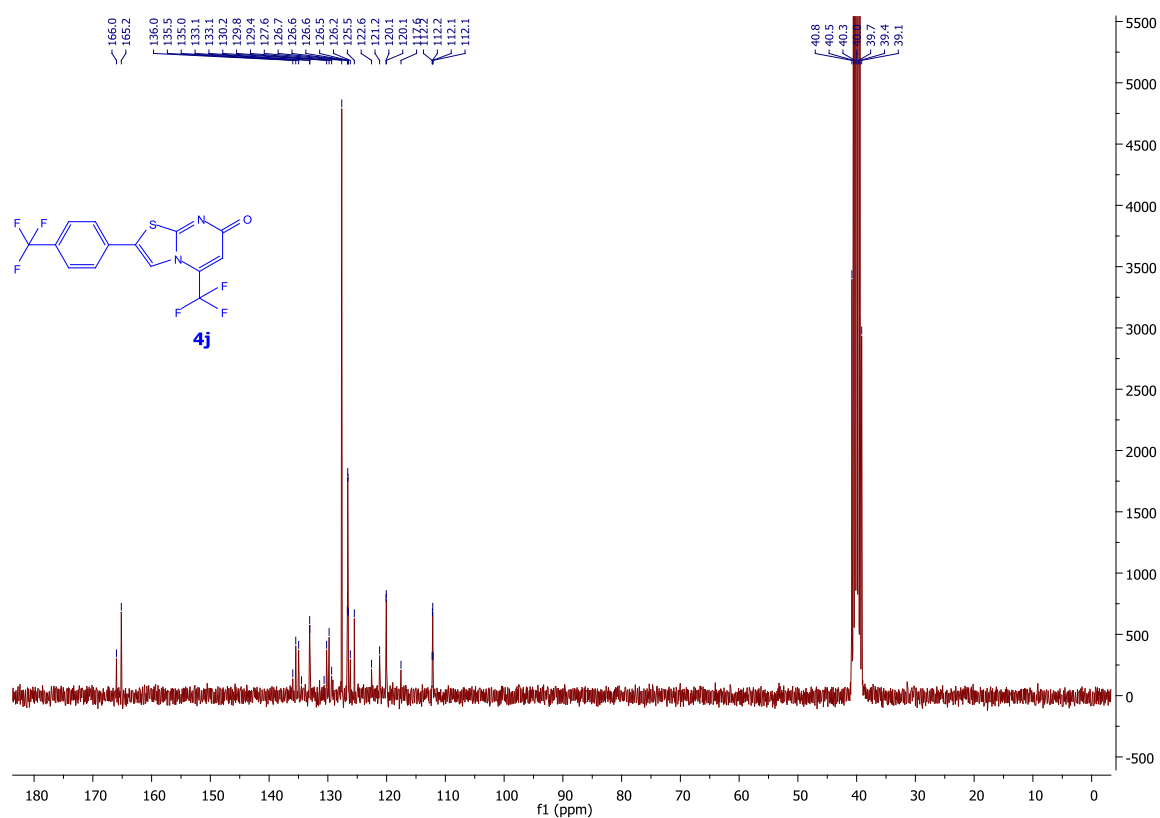
5-(trifluoromethyl)-2-(4-(trifluoromethyl)phenyl)-7*H*-thiazolo[3,2-*a*]pyrimidin-7-one (**4j**)

$^1\text{H}$  NMR (300 MHz,  $\text{MeOH-}d_4$ )



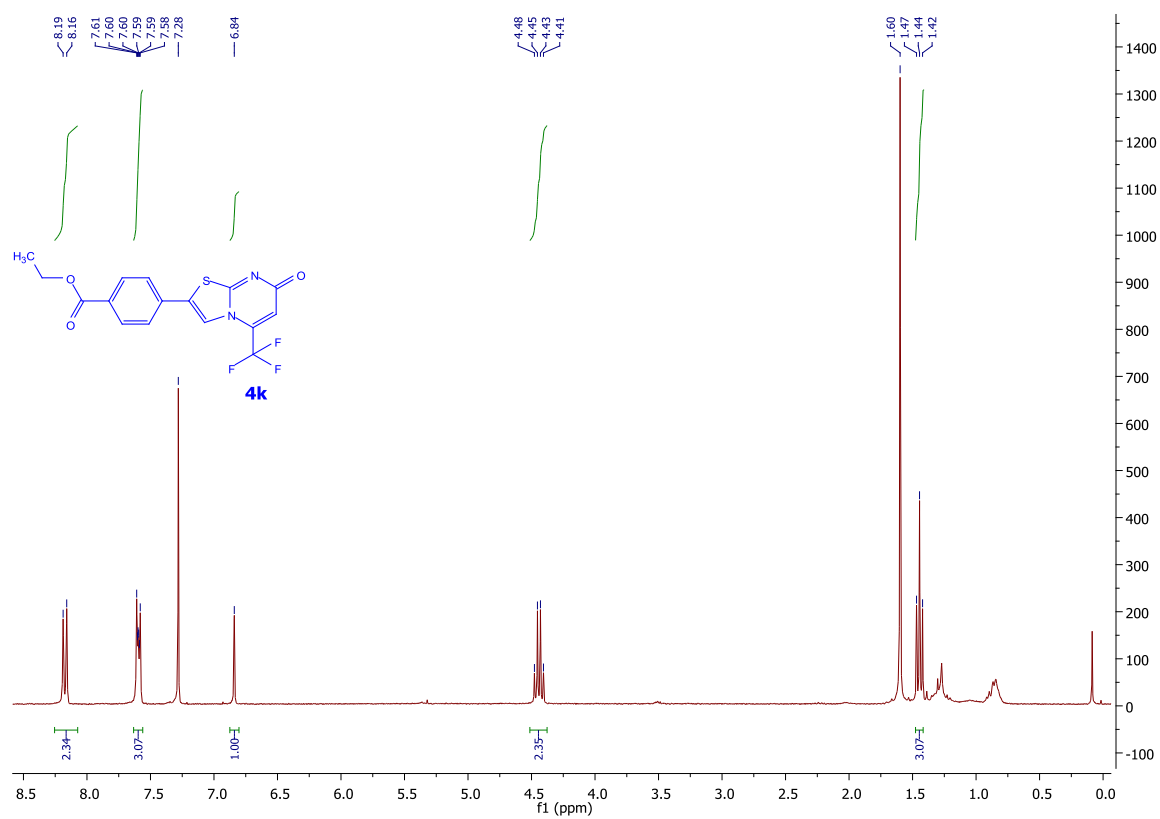
$^{19}\text{F}$  NMR (282 MHz,  $\text{MeOH-}d_4$ )



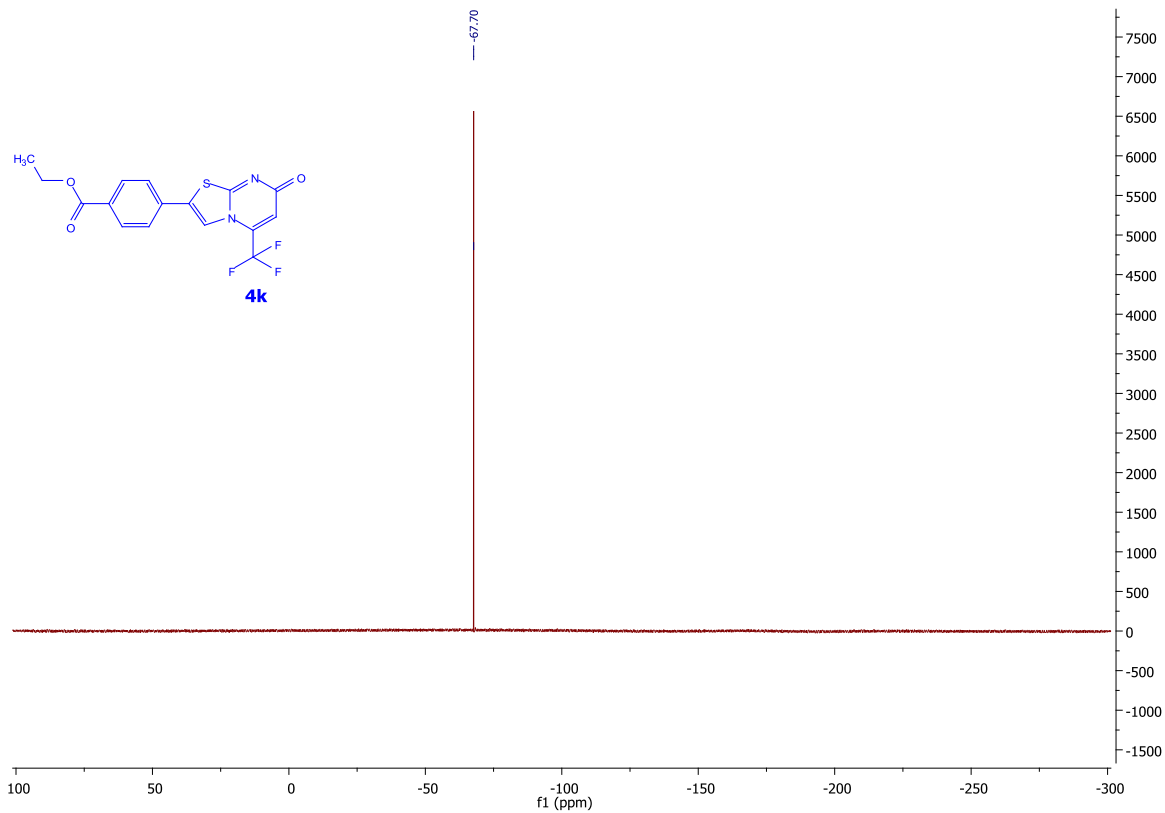
$^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ )

Ethyl 4-(7-oxo-5-(trifluoromethyl)-7*H*-thiazolo[3,2-*a*]pyrimidin-2-yl)benzoate (**4k**)

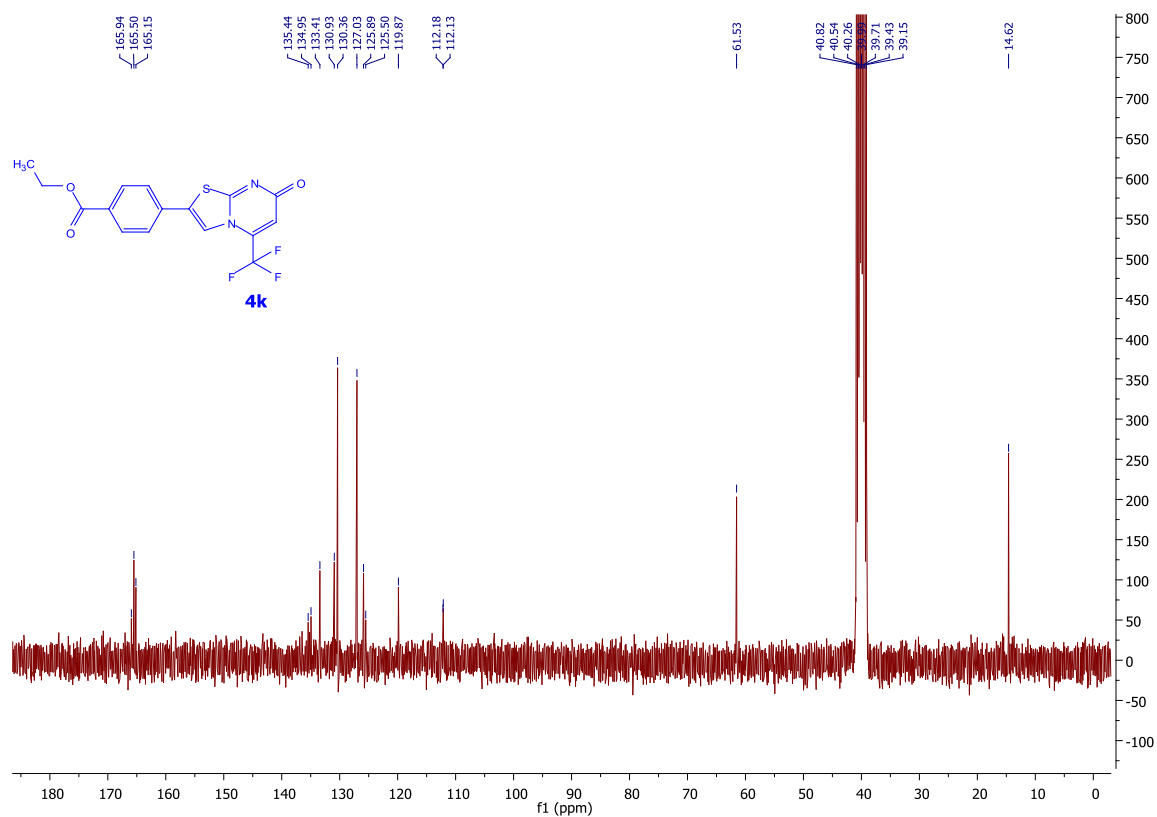
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)



<sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>)

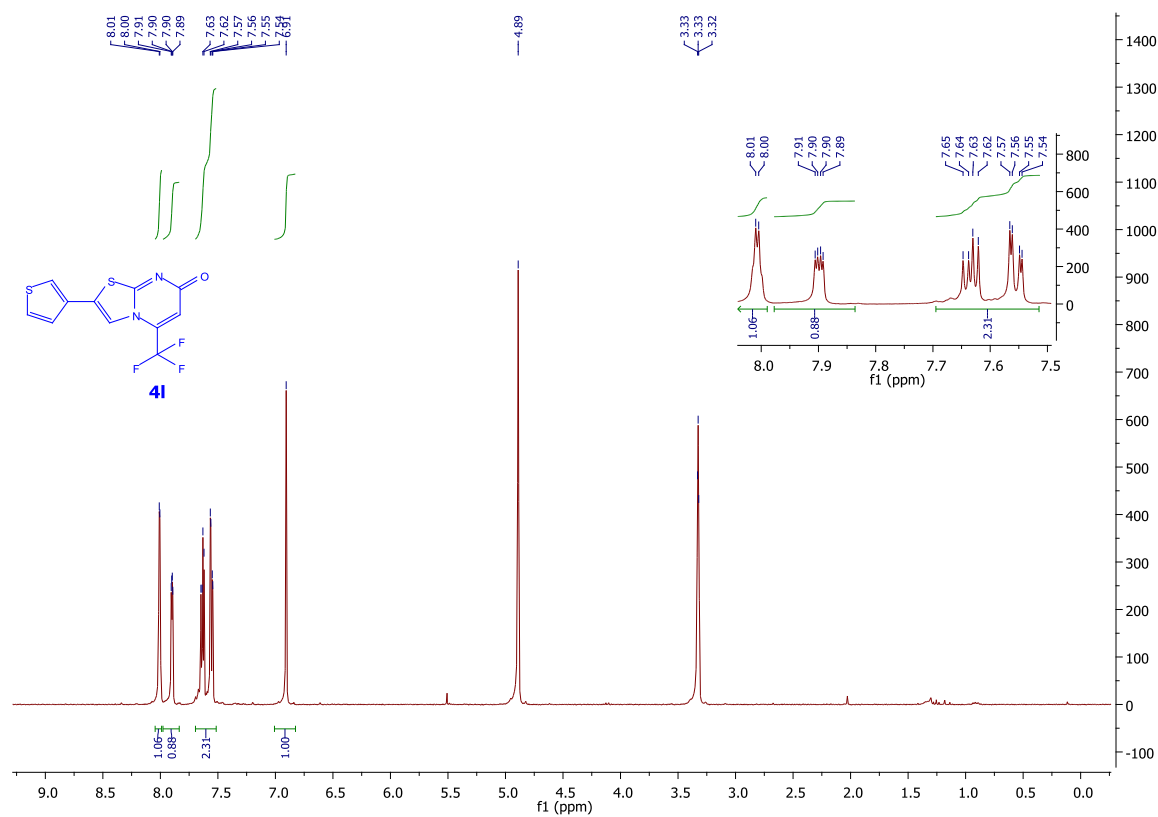


<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)

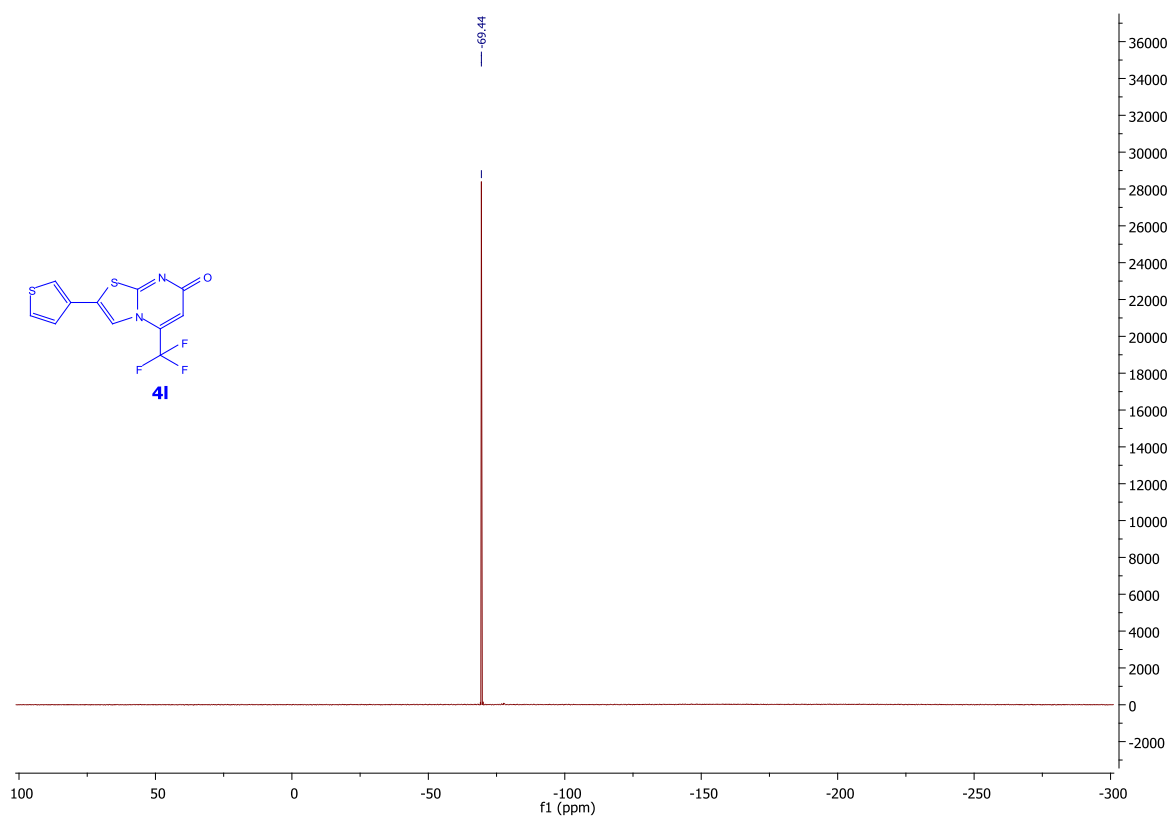


2-(thiophen-3-yl)-5-(trifluoromethyl)-7*H*-thiazolo[3,2-*a*]pyrimidin-7-one (**4l**)

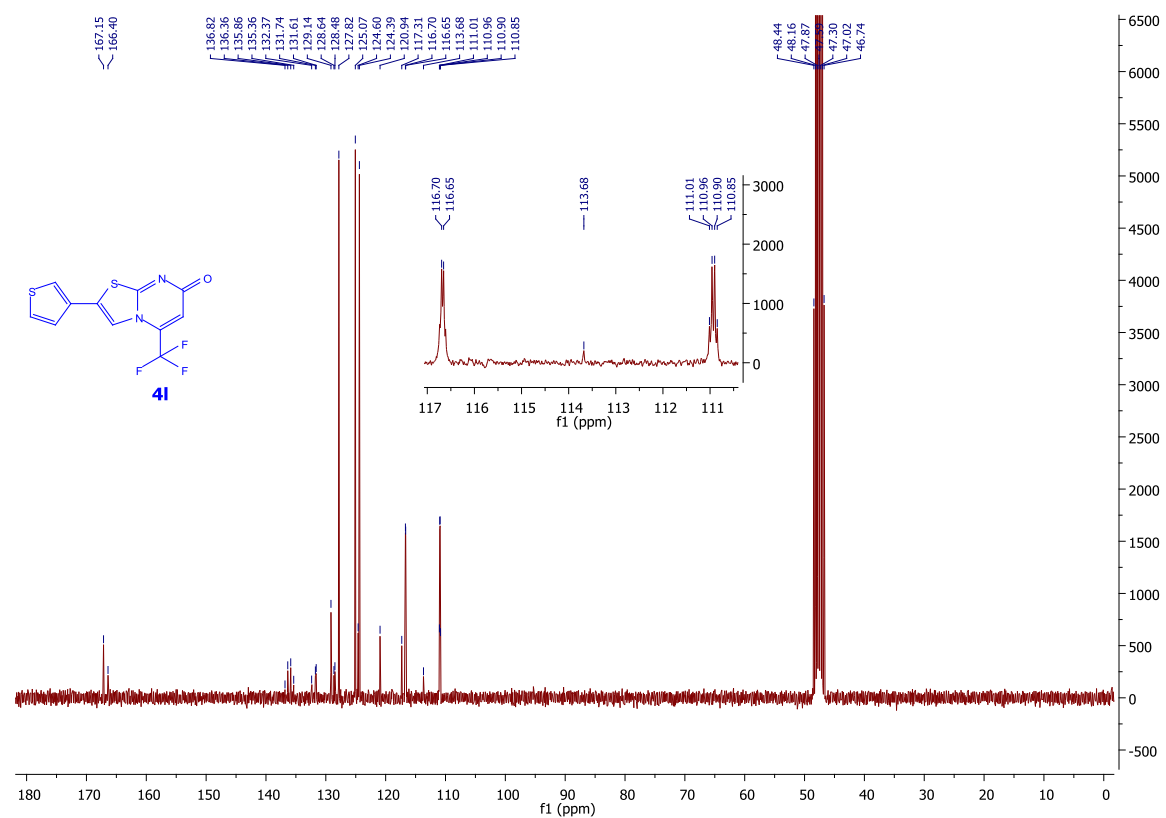
<sup>1</sup>H NMR (300 MHz, MeOH-*d*<sub>4</sub>)



$^{19}\text{F}$  NMR (282 MHz,  $\text{MeOH-}d_4$ )

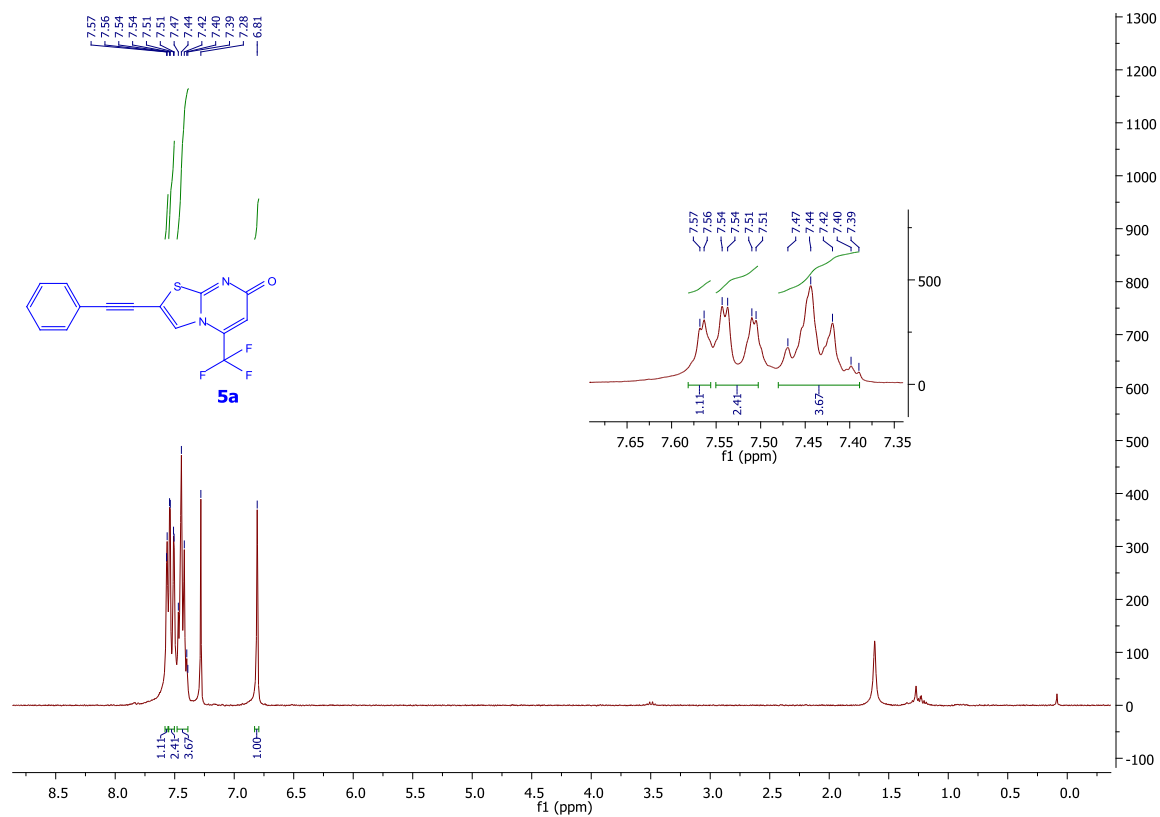


$^{13}\text{C}$  NMR (75 MHz,  $\text{MeOH-}d_4$ )

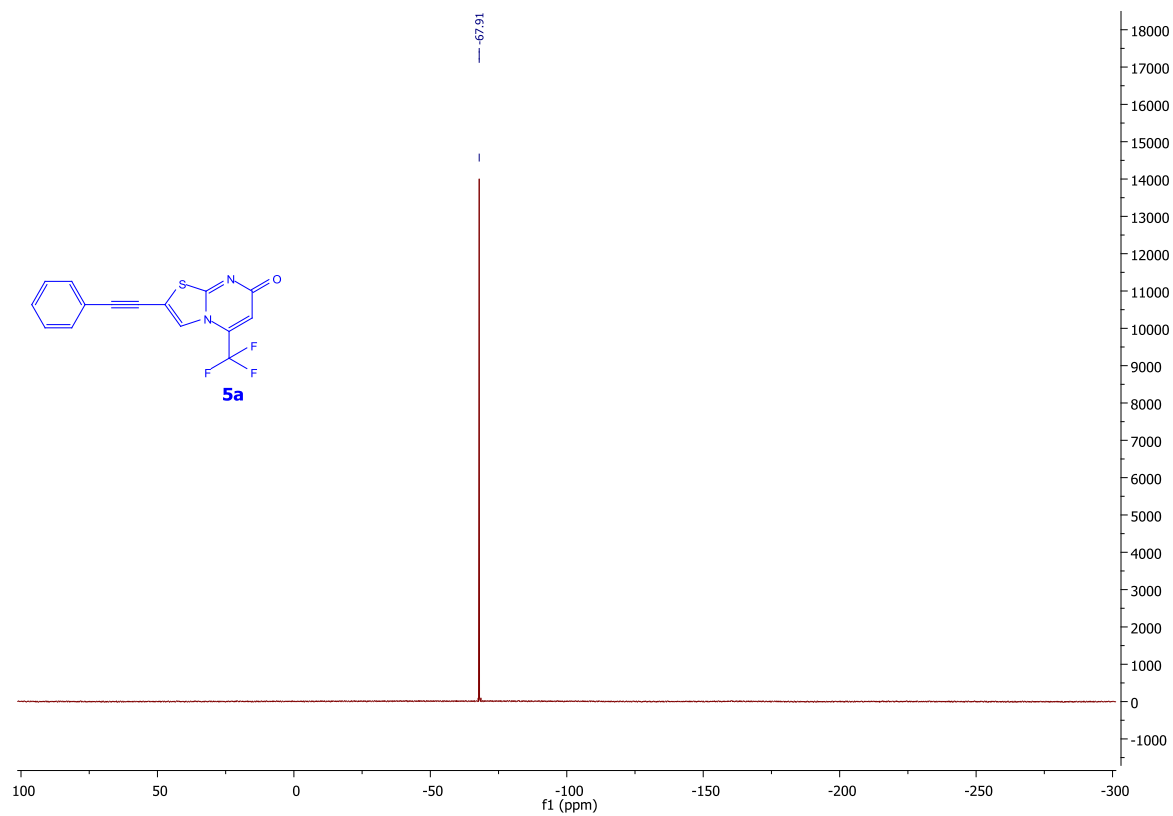


2-(phenylethynyl)-5-(trifluoromethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**5a**)

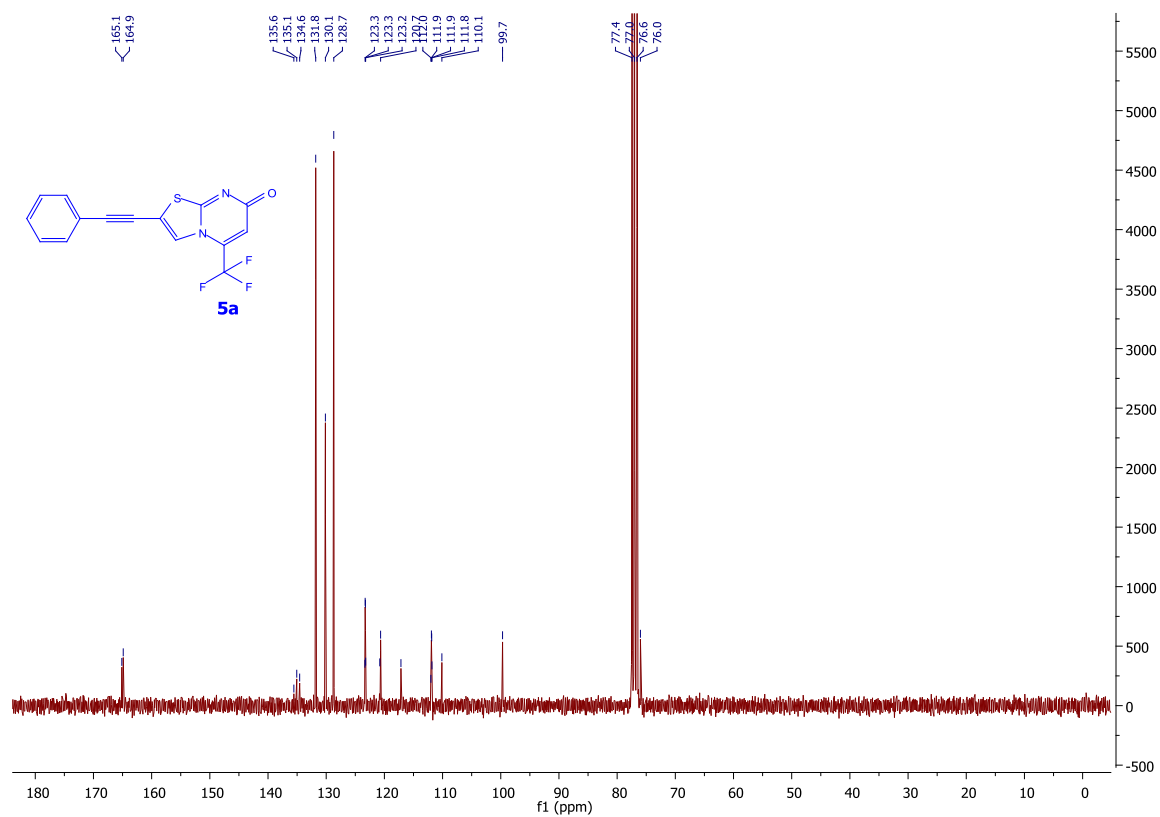
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



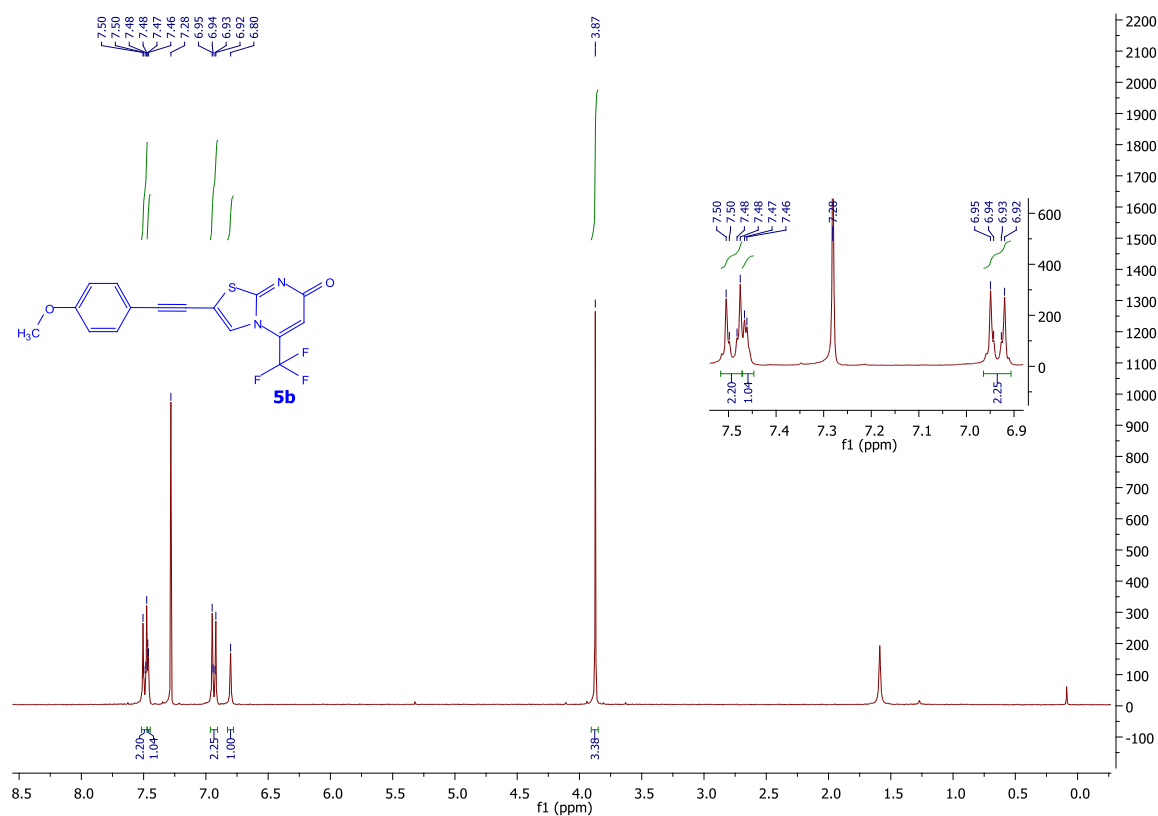
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)



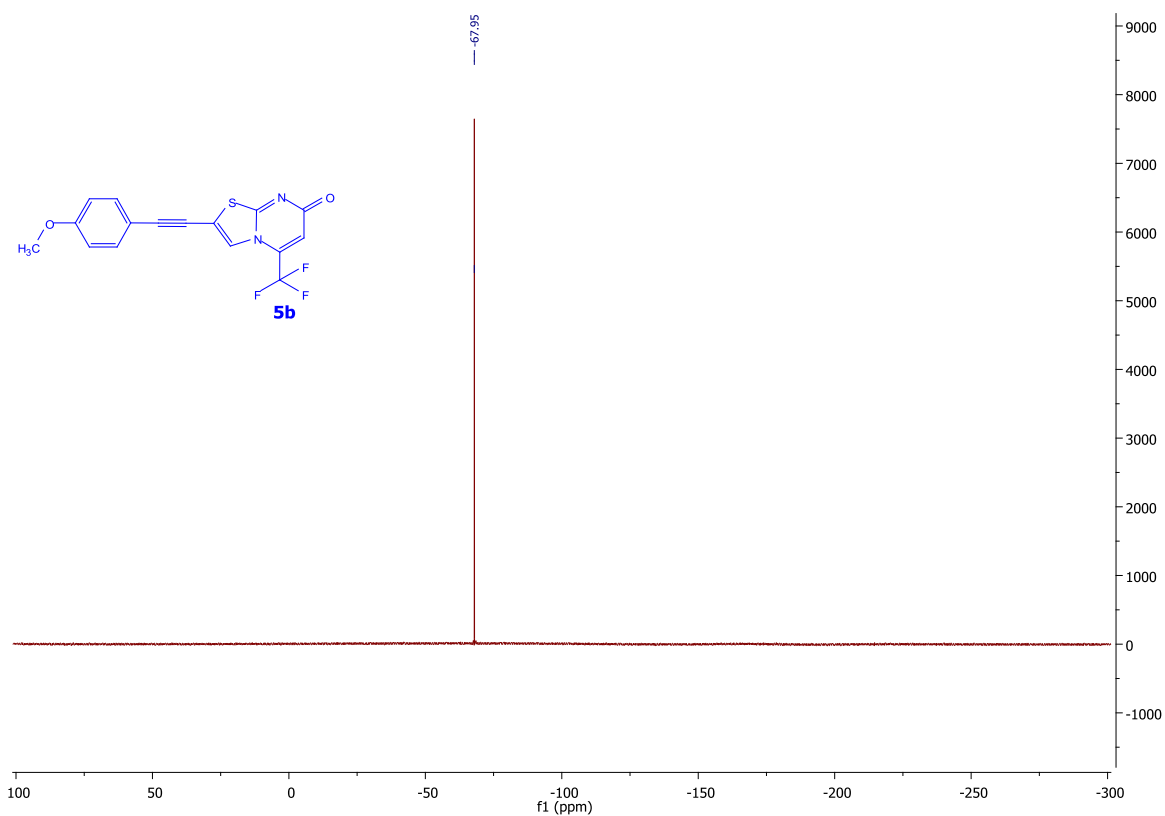
2-((4-methoxyphenyl)ethynyl)-5-(trifluoromethyl)-7*H*-thiazolo[3,2-*a*]pyrimidin-7-one (**5b**)



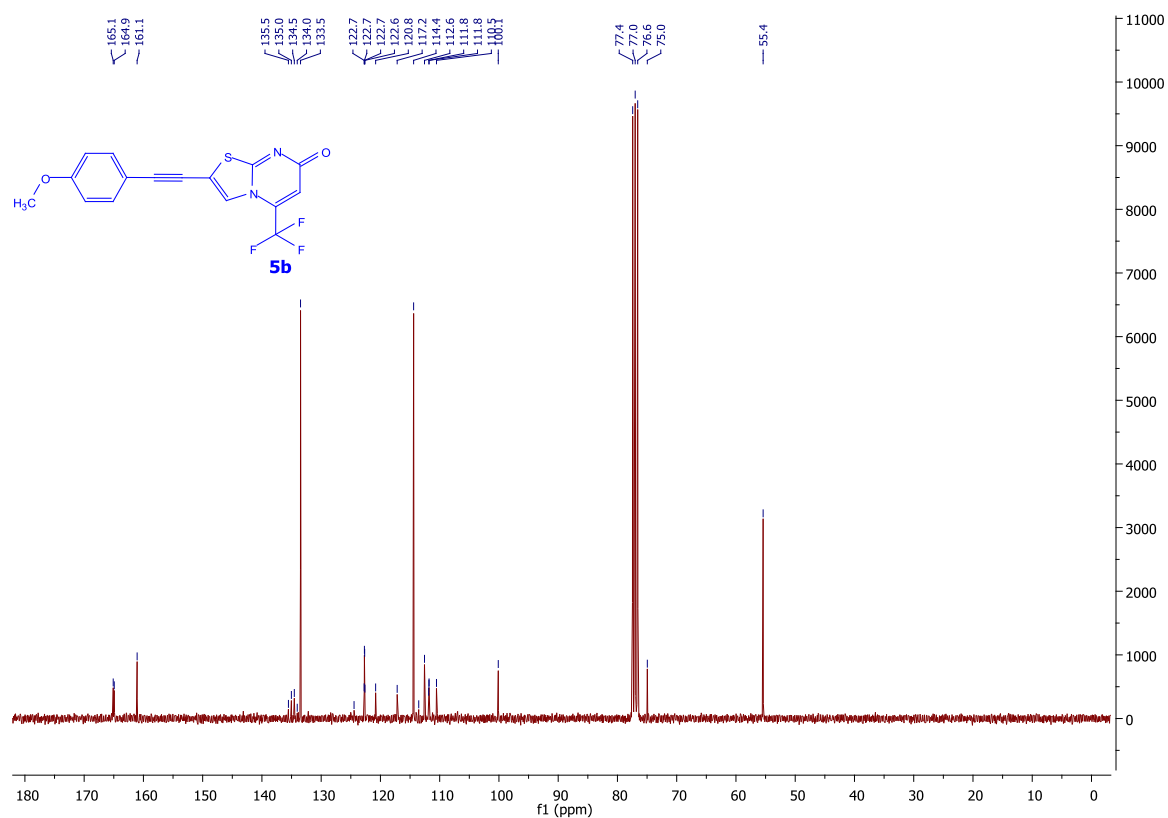
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

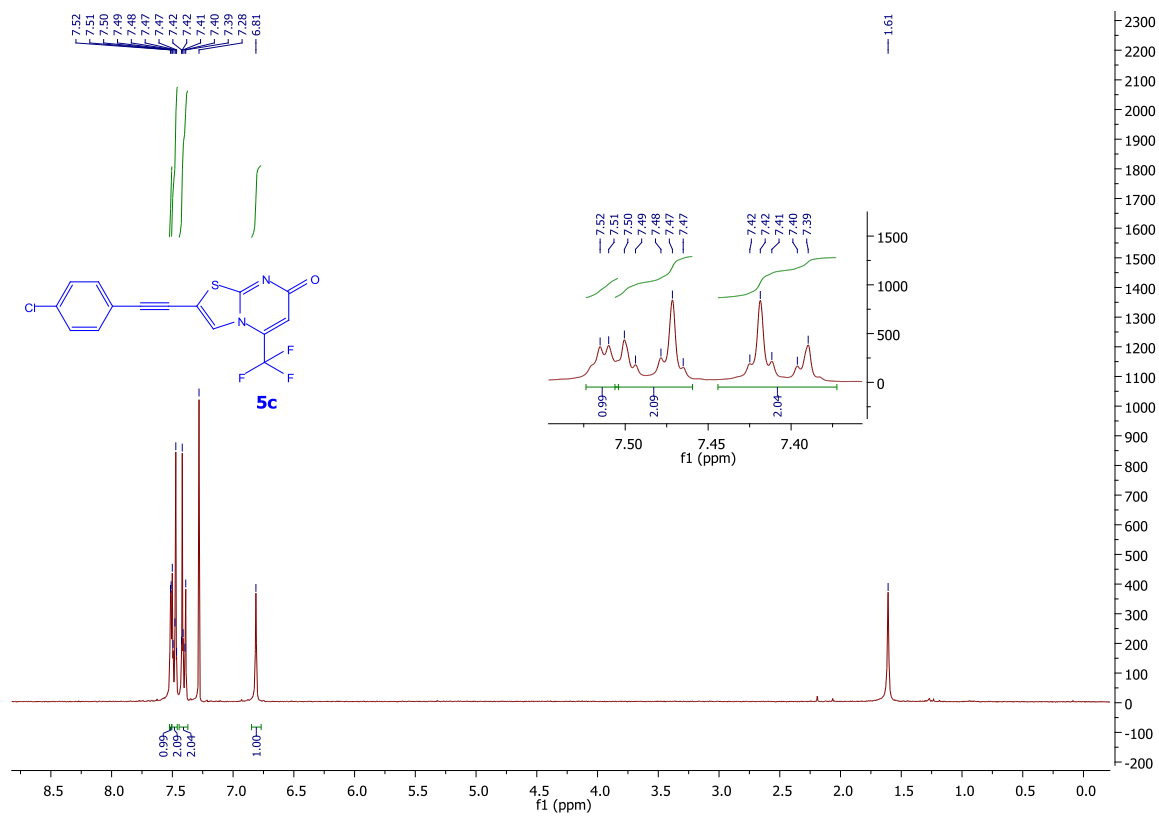


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

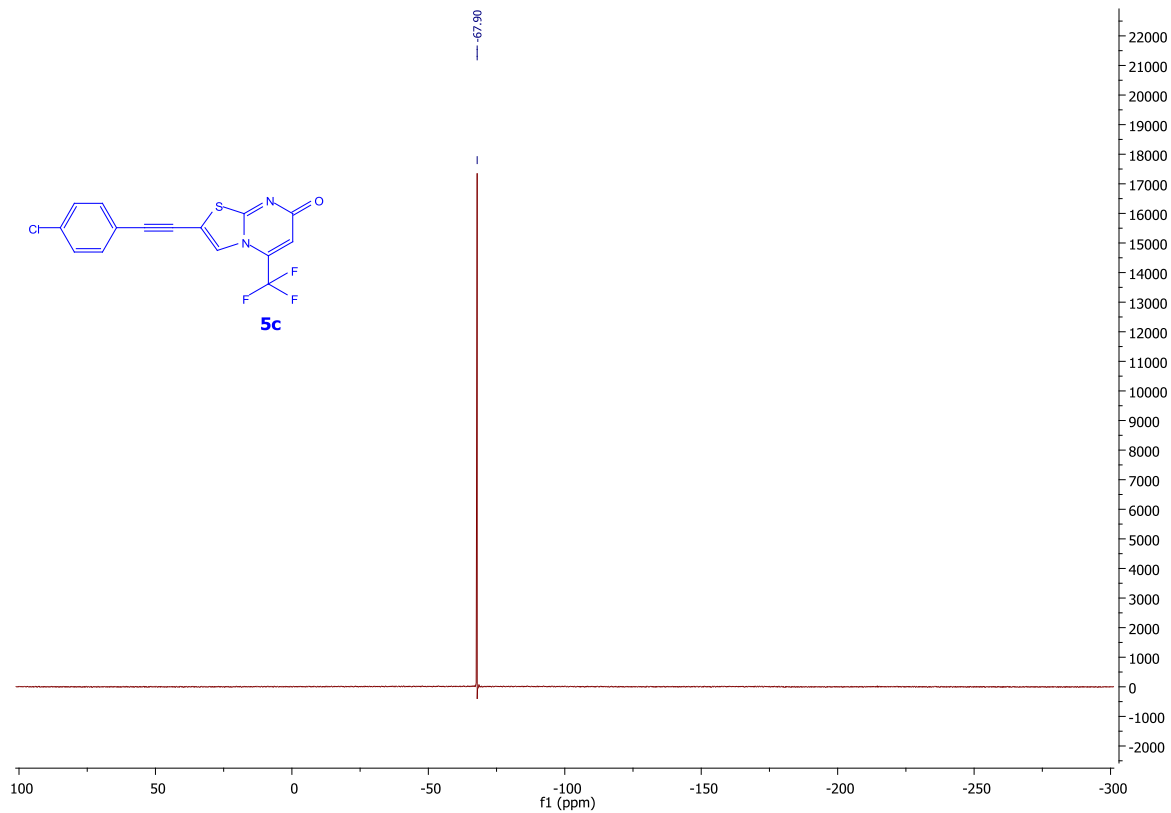


2-((4-chlorophenyl)ethynyl)-5-(trifluoromethyl)-7H-thiazolo[3,2-*a*]pyrimidin-7-one (**5c**)

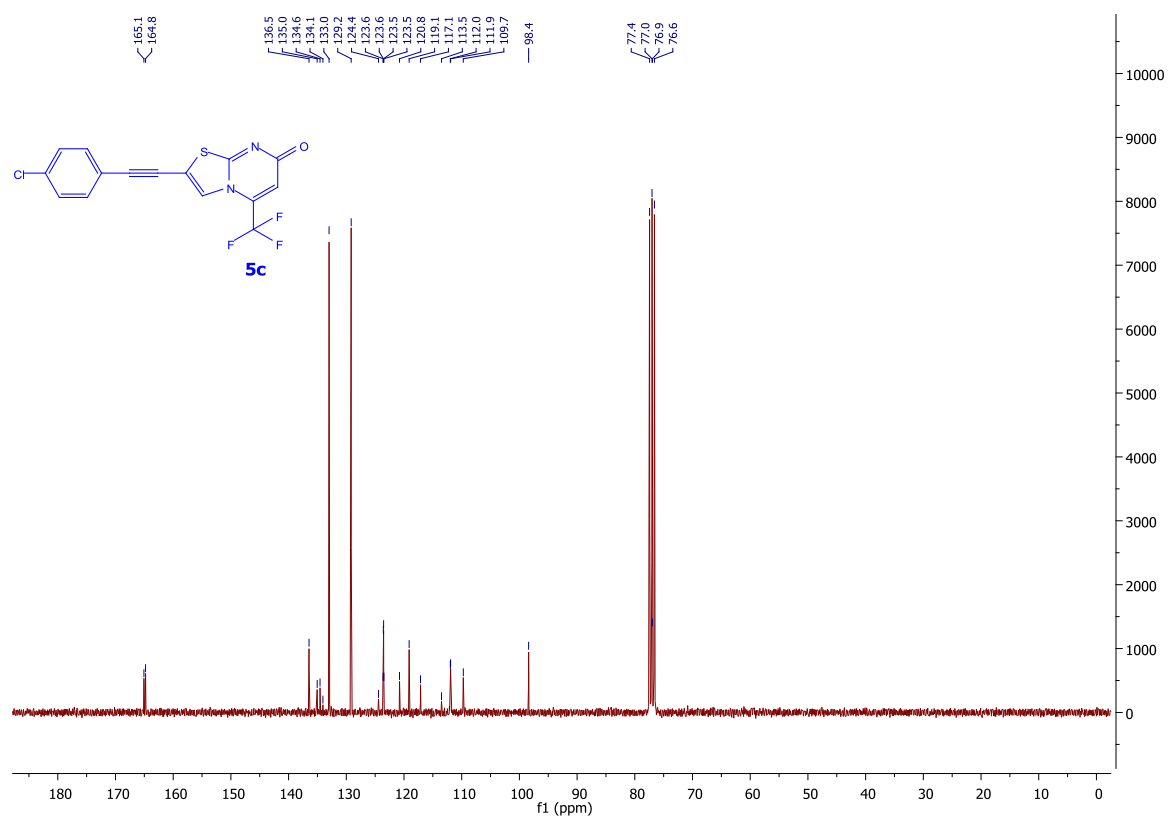
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



**<sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>)**

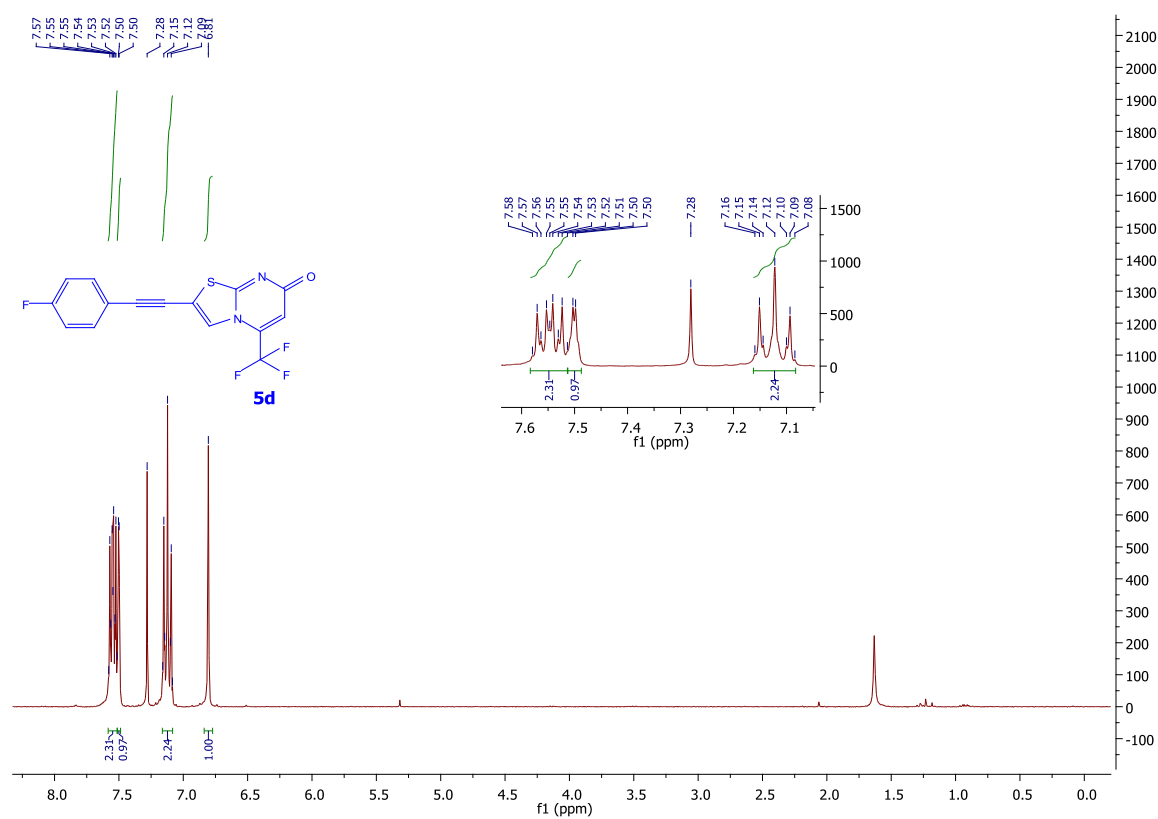


**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)**

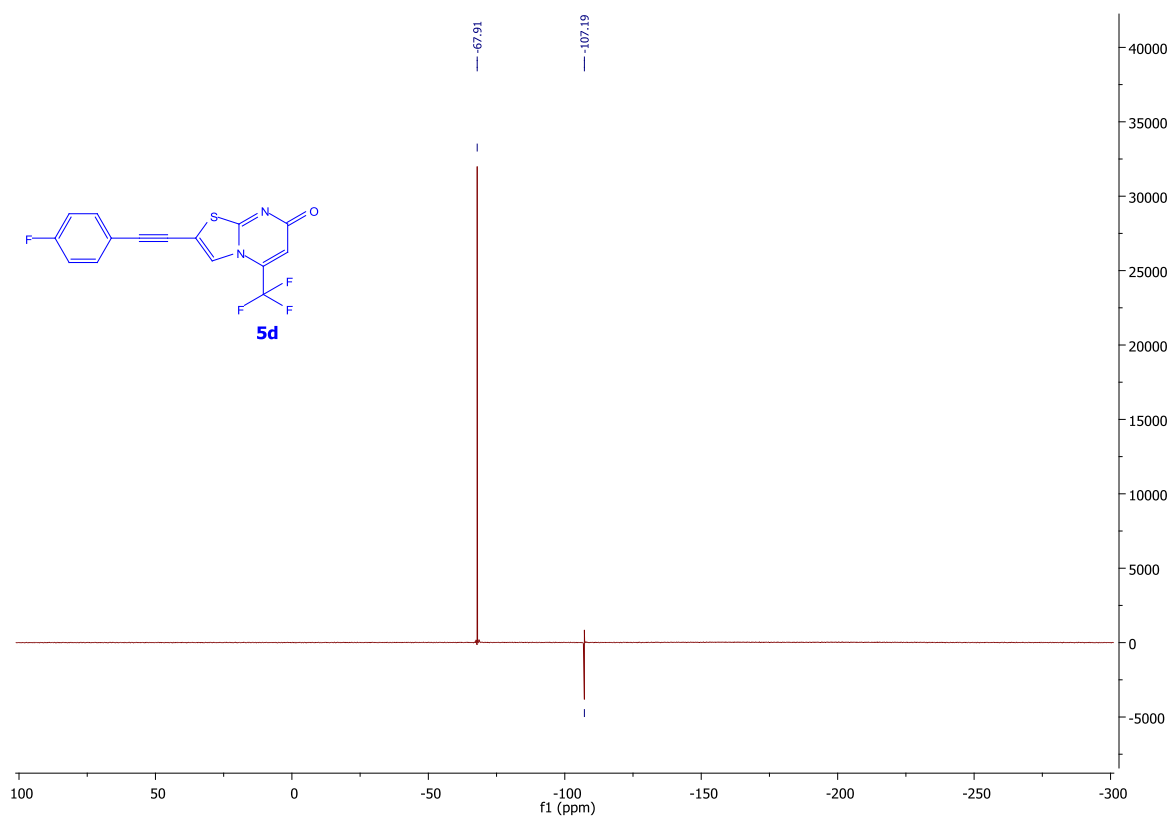


2-((4-fluorophenyl)ethynyl)-5-(trifluoromethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**5d**)

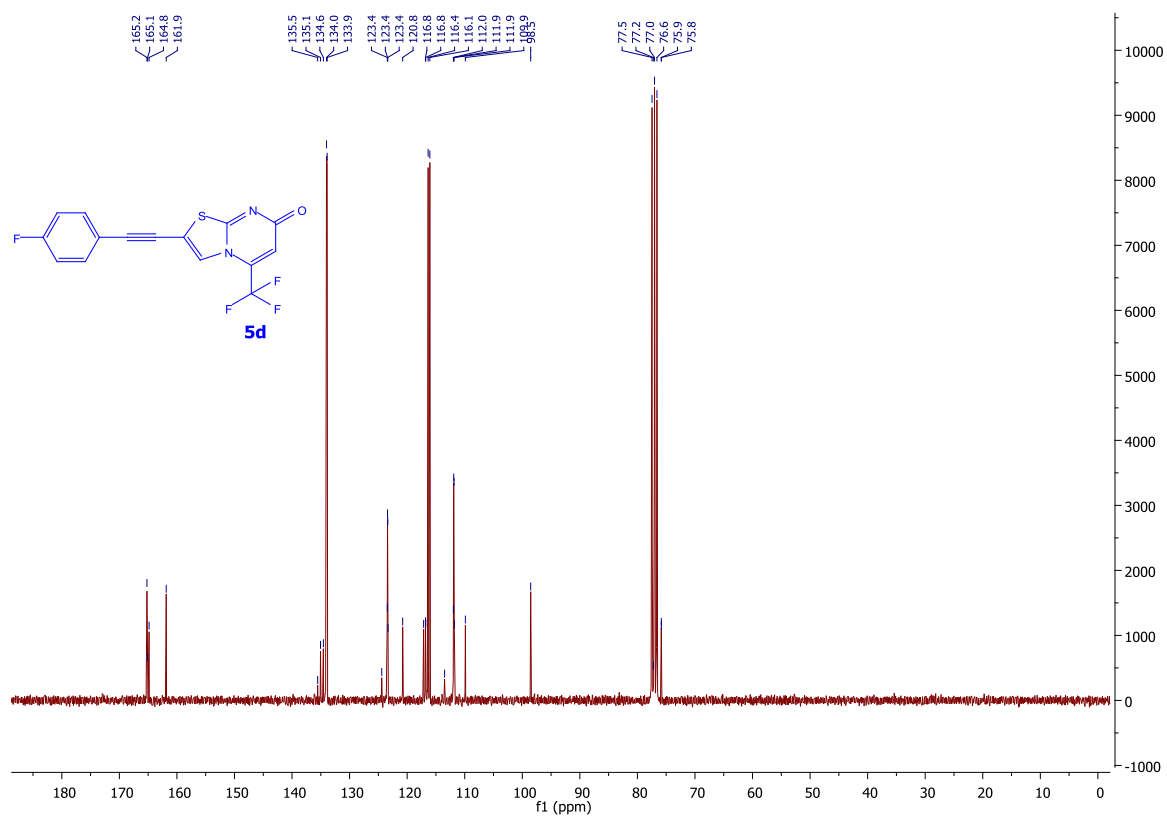
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

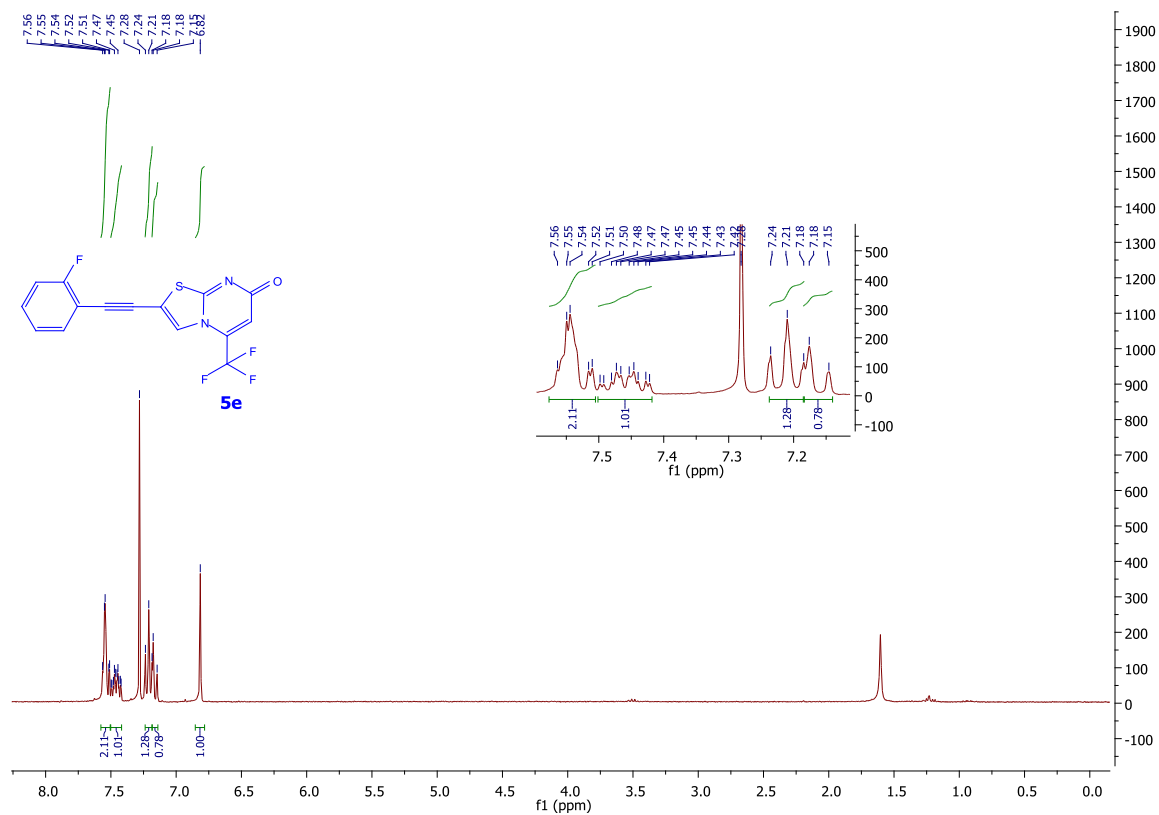


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

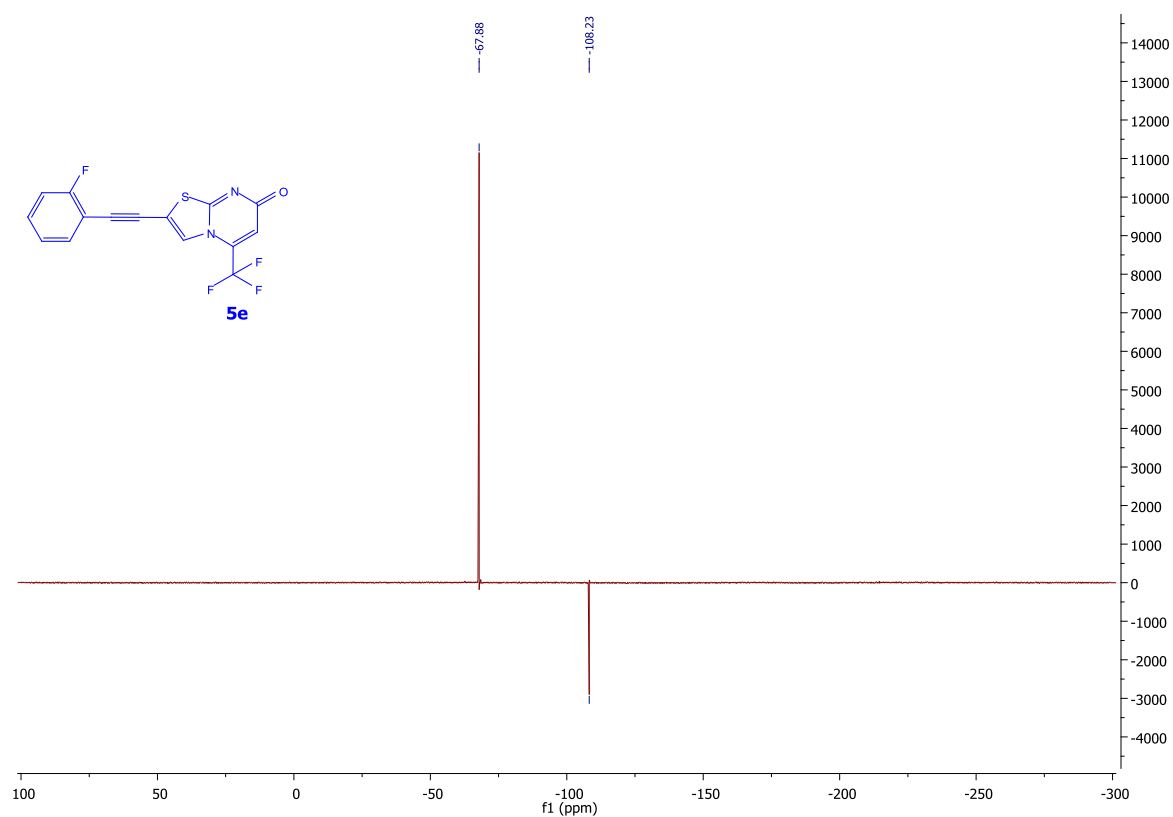


2-((2-fluorophenyl)ethynyl)-5-(trifluoromethyl)-7*H*-thiazolo[3,2-*a*]pyrimidin-7-one (**5e**)

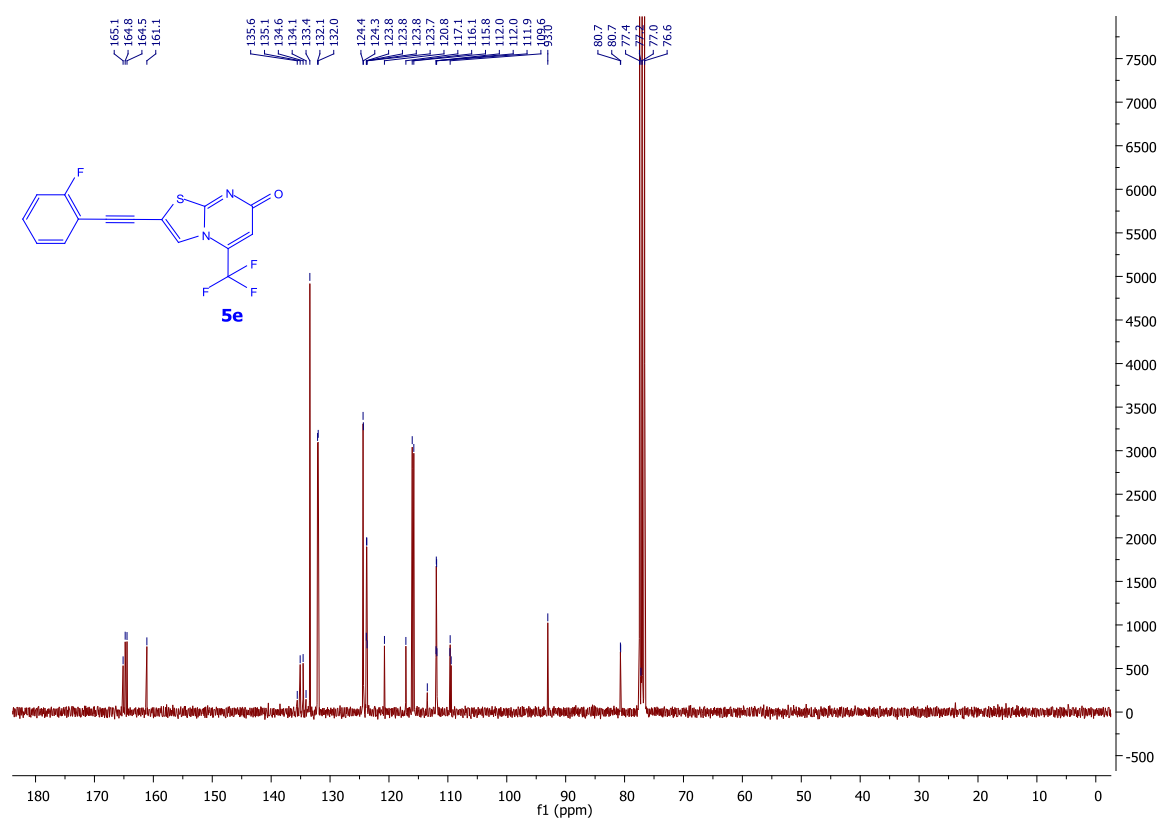
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

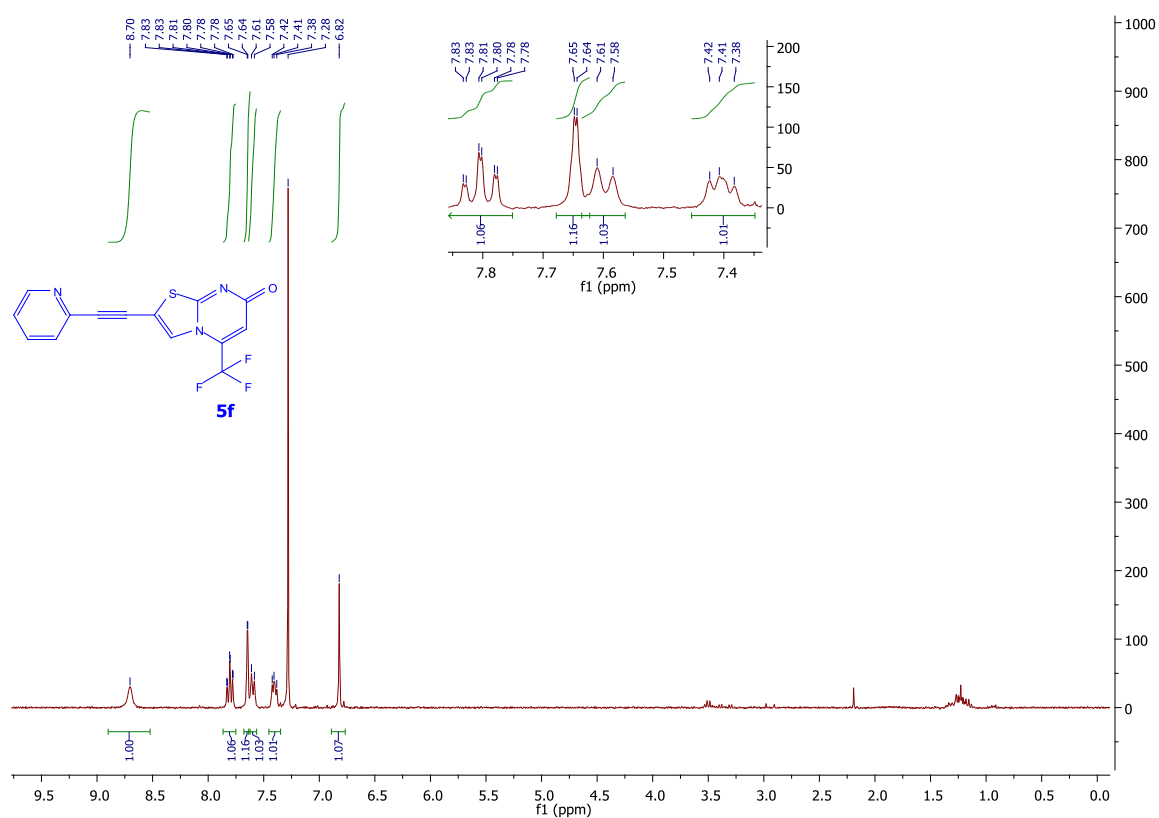


<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

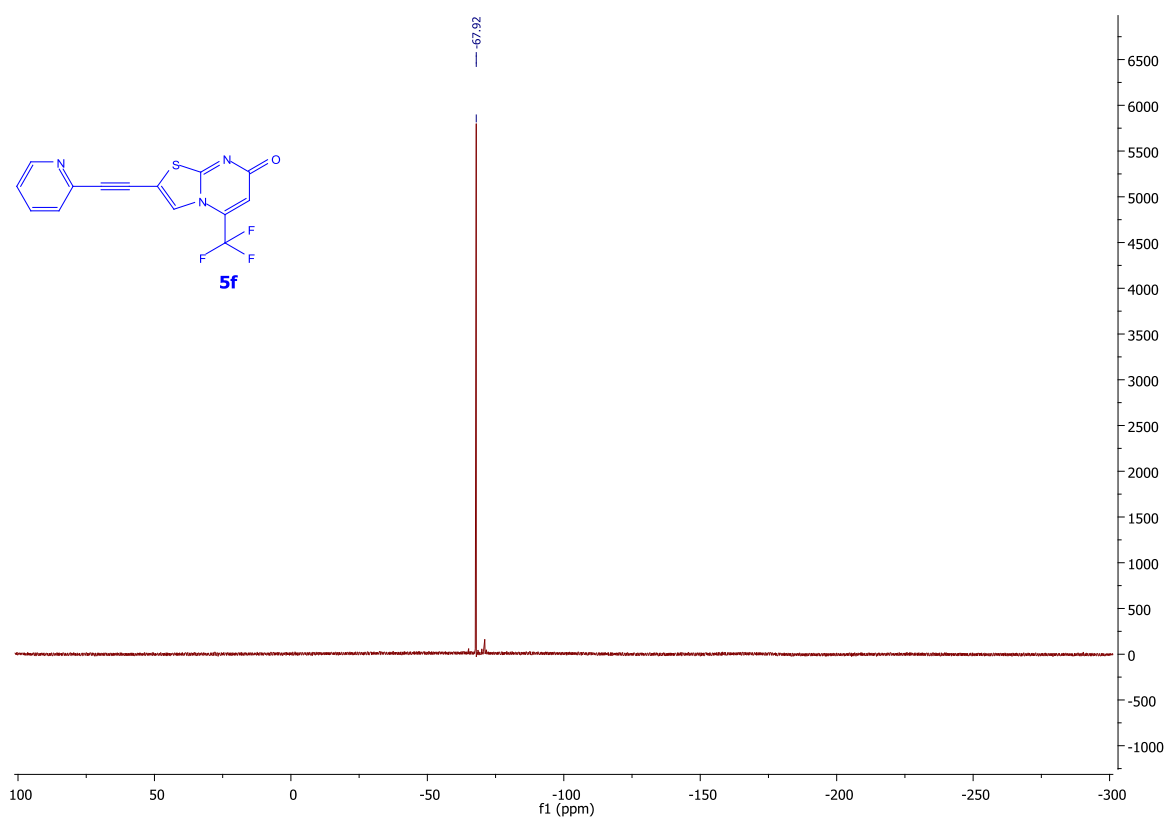


2-(pyridin-2-ylethynyl)-5-(trifluoromethyl)-7H-thiazolo[3,2-*a*]pyrimidin-7-one (**5f**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

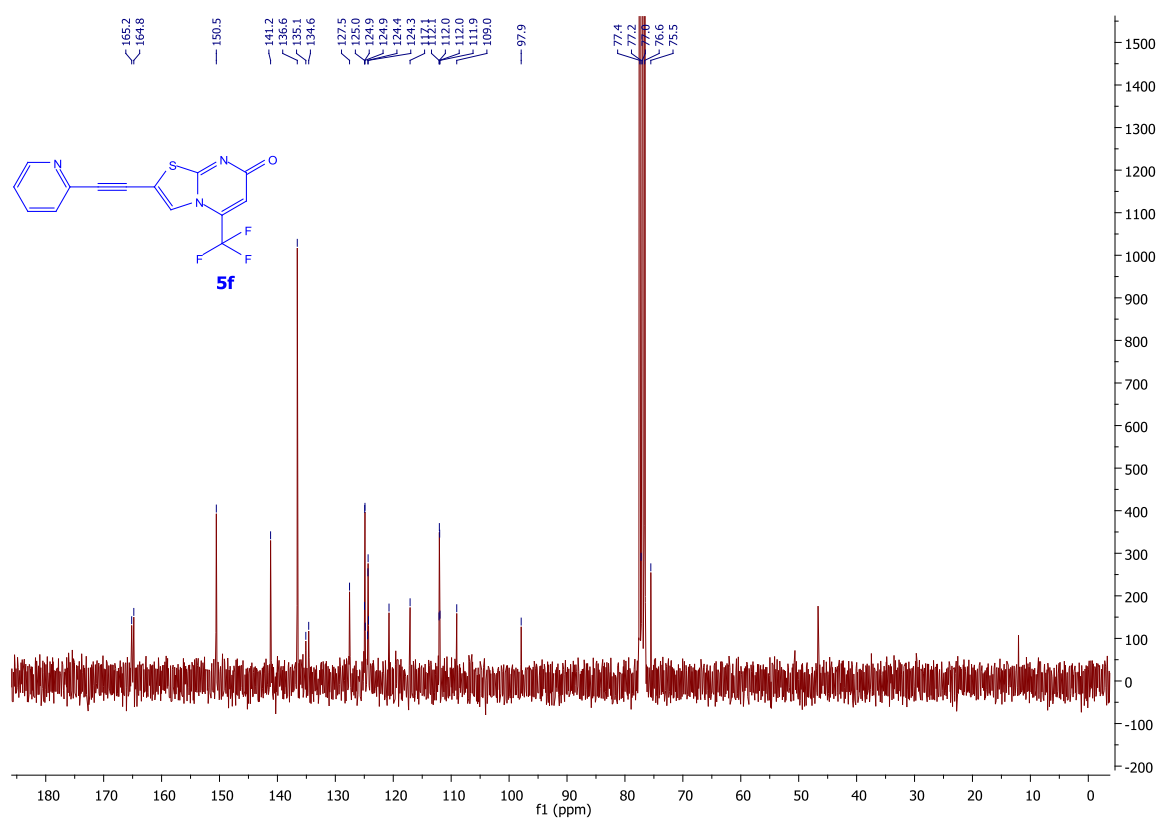


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



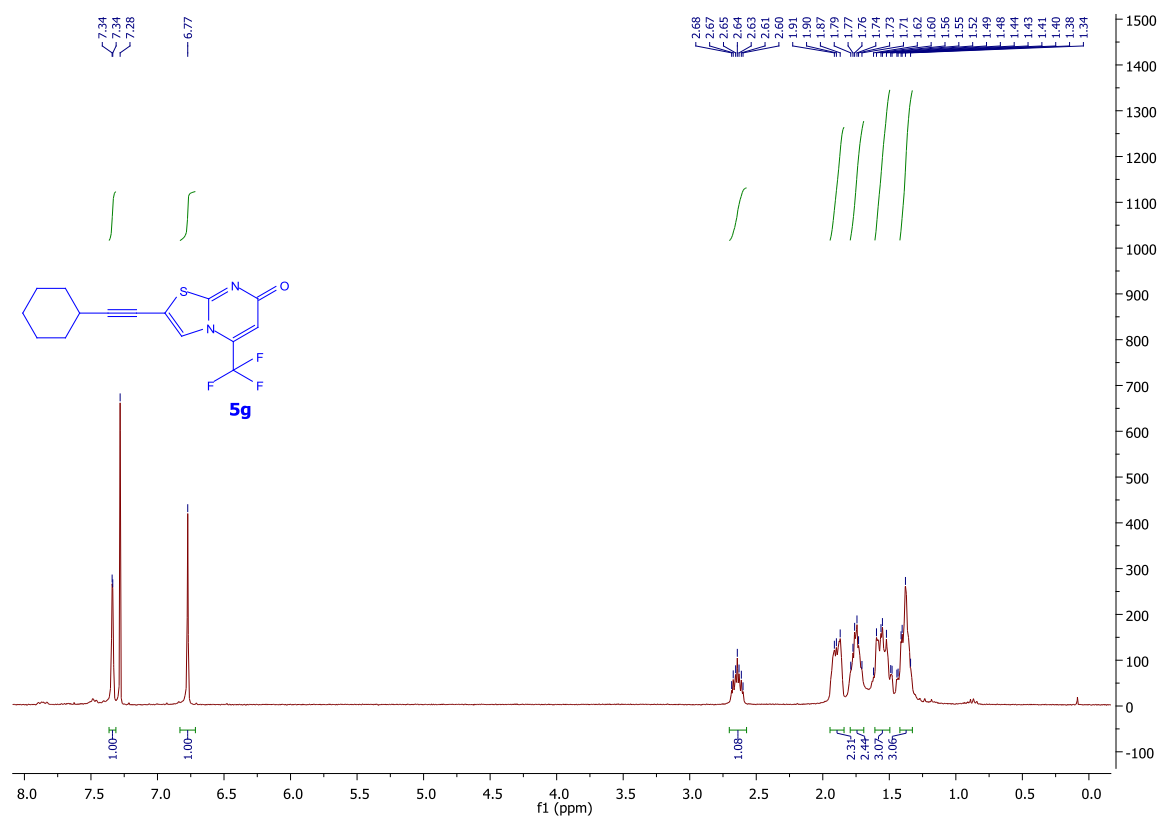


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

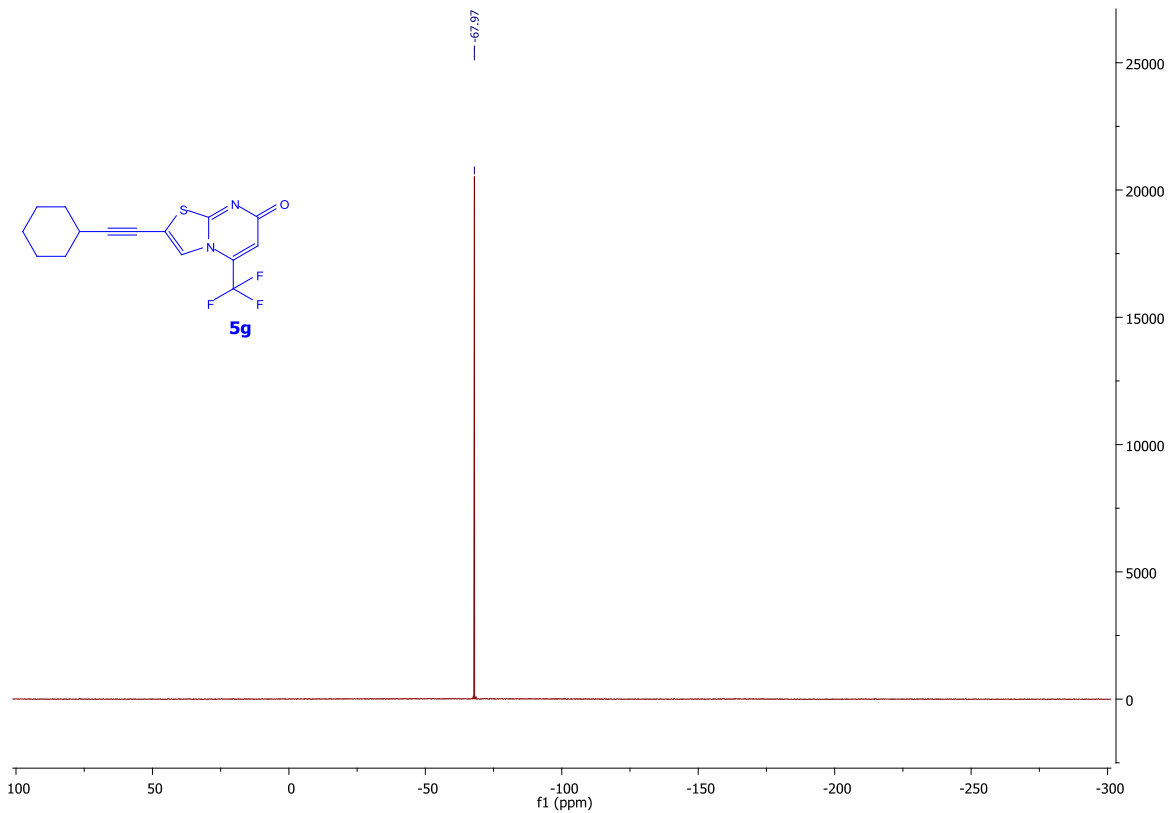


2-(cyclohexylethynyl)-5-(trifluoromethyl)-7H-thiazolo[3,2-*a*]pyrimidin-7-one (**5g**)

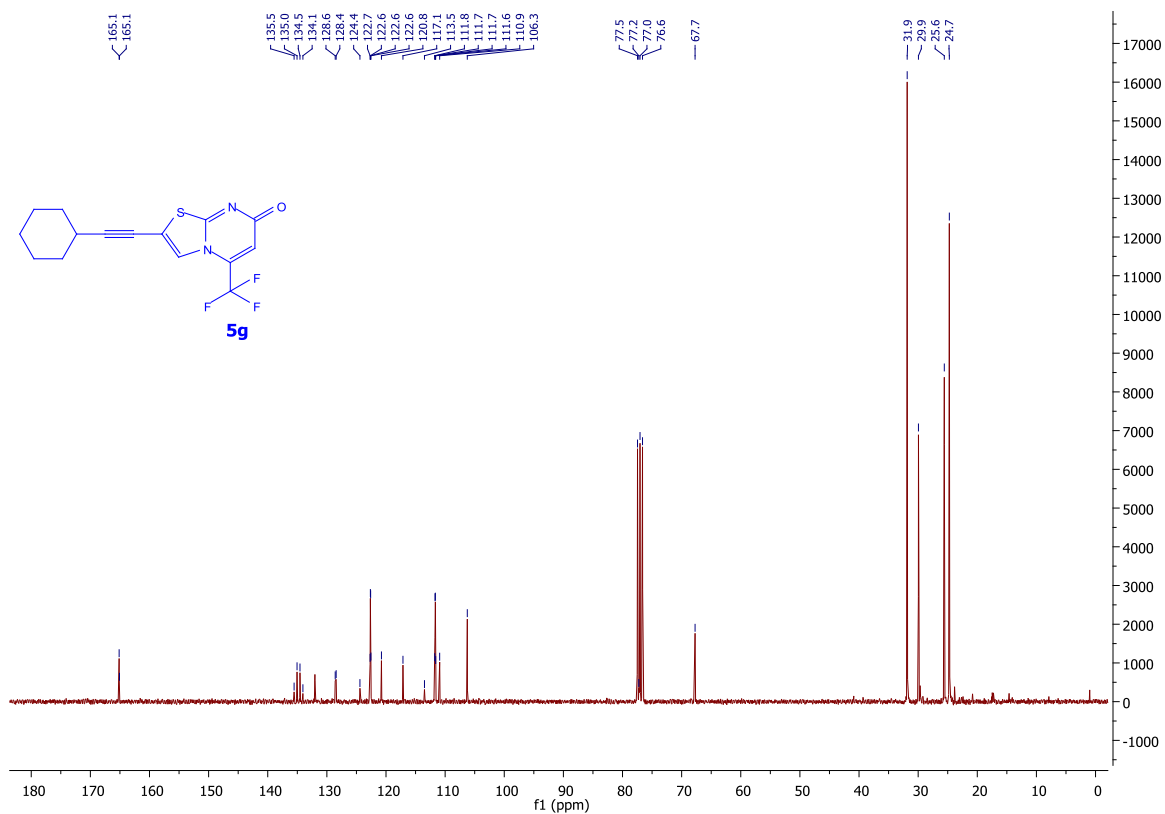
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



**<sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>)**

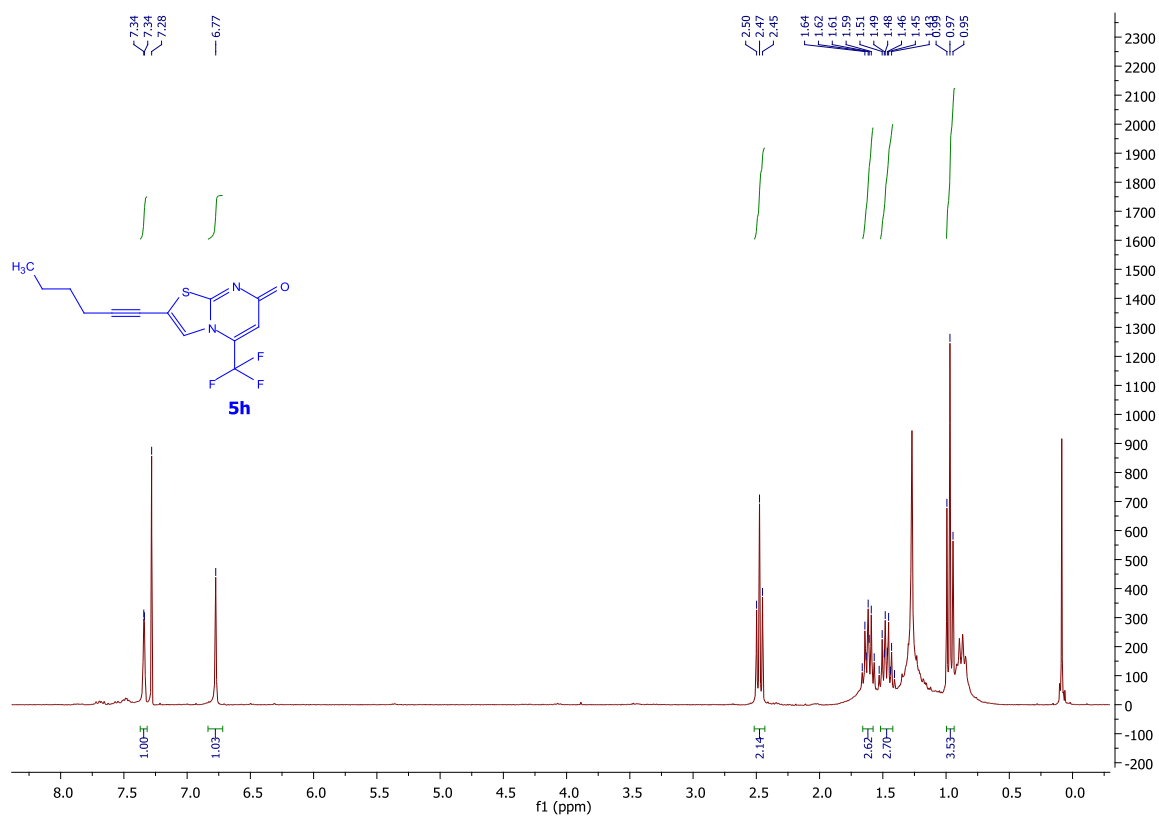


**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)**



2-(hex-1-yn-1-yl)-5-(trifluoromethyl)-7H-thiazolo[3,2-a]pyrimidin-7-one (**5h**).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)



$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

